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(54) Title: COLLECTION OF PROKARYOTIC DNA FOR TWO HYBRID SYSTEMS HELICOBACTER PYLORI PROTEIN-PROTEIN INTERACTIONS AND APPLICATION THEREOF

(57) Abstract: The present invention concerns collections of recombinant cell clones derived from a prokaryotic genome, more particularly from Helicobacter pylori genome, usable for two-hybrid systems and methods to produce such collections. The invention further relates to the identification of H. pylori protein-protein interactions and to the application of said collections of recombinant cell clones and said identified proteins interactions to the pharmaceutical and diagnostic field.

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AMENDED CLAIMS

[received by the International Bureau on 28 November 2000 (28.11.00); original claim 60 amended; remaining claims unchanged (2 pages)]

- b) a polynucleotide having the sequence identified by the reference indicated in the right column "SID®" in table III;
- c) fragment having at least 12 consecutive nucleotides of polynucleotide of a) or b), complement thereof, and RNA corresponding to said polynucleotide; and
- d) a polynucleotide having at least 80 % identity degree after alignment to a nucleic acid sequence of a polynucleotide of a) or b);

with the exception of the polynucleotides encoding the polypeptide having the sequence disclosed in the EMBL Data base document Accession number 025045.

- 61. Purified or isolated polypeptide selected from the group consisting of:
- a) a polypeptide having an amino acids sequence identified by the reference indicated in the right column "SID®" in table II, and fragment thereof having at least 5 consecutive amino acids; and
 - b) a polypeptide encoded by a polynucleotide according to claim 59 or 60.
- 62. Use of a polynucleotide according to claim 60 as a primer for amplification.
 - 63. Use of a polynucleotide according to claim 60 as a specific probe for detection.
 - 64. Cloning or expression vector containing a polynucleotide according to anyone of claims 59 and 60.
- 65. Vector according to claim 64, wherein the vector is the plasmid pACTIIst, pAS2ΔΔ or pP6.
- 66. Vector according to claim 64, wherein the vector is the plasmid selected from the group consisting of pT25, pKT25, pUT18 and pUT18C.
 - 67. Vector according to claim 64, wherein the vector is self replicated.
 - 68. Vector according to claim 64 or 67, wherein the vector is a viral vector.
- 69. Vector according to claim 68, wherein the vector is chosen between an adenovirus, AAV, a retrovirus, a proxivirus or an herpes virus.
- 70. Vector according to anyone of claims 64 to 69 including elements allowing expression and/or secretion of said polynucleotide in a host cell.
- Host cell transformed with a vector according to anyone of claims 64 to 70.

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- 72. Host cell according to claim 71, wherein the host cell is a prokaryotic cell.
- 73. Host cell according to claim 71, wherein the host cell is an eukaryotic cell.
- 74. Method for producing a polypeptide according to anyone of claims 45 and 61, comprising the steps of:
- a) cultivating a host cell according to anyone of claims 71 to 73 under conditions and in culture medium allowing the growth of said host cell and the expression of said polypeptide; and
- b) recovering said polypeptide directly from the culture medium or from said cultivated cell obtained in step a).
 - 75. Purified or isolated polypeptide obtained by the method according to claim 74.
- 76. A method for selecting an agent capable of modulating the proteinprotein interaction of a step of two polypeptides according to claim 45 comprising the steps of:
 - a) cultivating a recombinant cell clone containing a reporter gene expression of which is toxic for said recombinant cell clone and transformed with two plasmids wherein:
 - i) the first plasmid contains a nucleic construct comprising a nucleic sequence encoding a first hybrid polypeptide containing one of said two polypeptides and a DNA binding domain;
 - ii) the second plasmid contains a nucleic construct comprising a nucleic sequence encoding a second hybrid polypeptide containing the second of said two polypeptides and an activating domain capable of activating said toxic reporter gene when the first and the second hybrid polypeptides are interacting;
 - on a selective medium containing the agent to be tested and allowing the growth of said recombinant cell clone when the toxic reporter gene is not activated; and
 - b) selecting agent which is capable of inhibiting the growth of the recombinant cell clone cultivated in step a).
- 30 77. A method for selecting an agent capable of modulating the protein-protein interaction of a set of two polypeptides according to claim 45 comprising the steps of:

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specific site on the DNA and a domain that is necessary for activation (Keegan et al., 1986, Science, 231(4739): 699-704 Separation of DNA binding from the transcription activating function of eukaryotic regulatory protein).

To date however, the two-hybrid assay system has not been specifically applied to the systematic study of prokaryotic protein-protein interactions although number of diseases are due to prokaryotic microorganisms.

One of the prokaryotic microorganisms presenting a great interest is *Helicobacter* pylori. Helicobacter pylori (H. pylori) is a microaerophilic, Gram negative, slow growing, spiral shaped and flagellated organism. H. pylori has been first isolated in 1983 from gastric biopsy specimen of patient with chronic gastritis (Marshall et al., 1984, Lancet, i:1311-1314, Unidentified curved bacilli in the stomach of patients with gastritis and peptic ulceration).

Helicobacter pylori has become identified as a primary cause of chronic gastroduodenal disorders, such as gastritis, dyspepsia, and peptic ulcers, in humans. Studies have shown (Labigne et al.) that H. pylori can be successfully eradicated by a treatment combining two antibiotics with a proton pump inhibitor. However, few antibiotics are active against H. pylori, and antibiotic-resistant strains have begun to appear.

H. pylori strain n° 26695 genome has been studied by Tomb et al. (Tomb et al., 1997, Nature, vol. 388, 539-547, The complete genome sequence of the gastric pathogen Helicobacter pylori). This strain's genome consists of a circular chromosome with a size of 1,667,867 bp, average G + C content of 39 %, and 1590 predicted coding sequences (open reading frames or "ORF").

The bacterial factors necessary for colonization of the gastric environment, and for virulence of this pathogen, are poorly understood. Examples of known virulence factors are:

- Enzymes involved in neutralizing the acid gastric pH: the multisubunit urease is a characteristic enzyme that is crucial for survival in acidic pH and for successful colonization of the gastric environment, a site that few other microbes can colonize (Labigne et al., WO 93/07273, *Helicobacter pylori* genes necessary for the regulation and maturation of urease, and use thereof). Genes encoding ureases have been located

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on a 34 kb chromosome fragment and comprise ureA, ureB, ureC, ureD, ureE, ureF, ureG, ureH and ureI.

- Bacterial flagellar proteins responsible for motility across the mucous layer (Hazell et al., 1986, J. Inf. Dis., 153, 658-663 Campylobacter pyloridis and gatritis: association with intracellular spaces and adaptation to an environment of mucus as important factors in colonization of the gastric epithelium; Leying et al., 1992, Mol. Microbiol., 6, 2863-2874 Cloning and genetic characterization of Helicobacter pylori flagellin gene): flagellar filaments biosynthesis comprises A and B flagellins and the filament cap. These two biosyntheses are regulated by flbA gene (Suerbaum et al., French patent application, 1995, N 2 736 360, Cloning and characterization of flbA gene of Helicobacter pylori, aflagellated strains production).

- Two other essential toxins for virulence are VacA and CagA:

- VacA is a *H. pylori* toxin that induces the formation of large acidic vacuoles in host epithelial cells. These large vacuoles originate from massive swelling of membranous compartments of late stages of the endocytic pathway (de Bernard et al., 1997, Microbiology, 26(4), 665-674, *Helicobacter pylori* toxin VacA induces vacuole formation by acting in the cell cytosol). Proof for receptor-mediated interaction with VacA has been made by Pagliaccia et al.; m2 allele of vacA gene has always been described as inactive in the in vitro HeLa cell assay, however, the m2 allele is associated with peptic ulcer and is prevalent in populations in which peptic ulcer and gastric cancer have high incidence (Pagliaccia et al., Proc. Natl. Acad. Sci. U.S.A, 1998, 95(17), 10212-10217, The m2 form of the *Helicobacter pylori* cytotoxin has cell type-specific vacuolating activity).

- CagA is one of the proteins encoded by the "cag pathogenicity island" (Spohn et al. 1997, Molecular Microbiology, 26(2), 361-372, Transcriptional analysis of the divergent cagAB genes encoded by the pathogenicity island of *Helicobacter pylori*) found in *H. pylori* strains isolated from most patients with peptic ulcer disease and adenocarcinoma. CagA is produced by 50-60 % of *H. pylori* strains; it is a high molecular weight (120-140 kDa) superficial protein and an immunodominant antigen with unknown function. *H. pylori* strains that produce CagA protein have two genes cagB and cagC (36 and 101 kDa proteins, respectively). These genes are highly

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associated with duodenal ulcers (Blaser et al. 1996, WO 96/12825, cagB and cagC genes of *Helicobacter pylori* and related methods and compositions).

- Other virulence factors are : several gastric tissue-specific adhesins (Boren et al., 1993, Science, 262, 1892-1895).

Therapeutic agents are currently available that eradicate *H. pylori* infections *in vitro*. However, methods employing antibiotic agents result in the emergence of bacterial strains which are resistant to these agents.

As number of diseases are due to prokaryotic microorganisms, there is a great need for new tools directed to the functional and global study of these newly characterized complete or partial genome, particurlarly *Escherichia coli* genome, but also of pathogenic microorganisms such as *H. pylori*, *Staphylococcus aureus* and *Streptococcus pneumoniae* genomes.

In addition to the need for these new tools, there is also and especially a need to find new E. coli, H. pylori, S. aureus and S. pneumoniae protein-protein interactions for the development of more effective and better targeted therapeutic.

Summary of the invention

The present invention relates to a method for producing a collection of recombinant cell clones usable for two-hybrid systems containing genomic DNA fragments of prokaryotic micro-organism, particularly of E. coli, H. pylori, S. aureus and S. pneumoniae, to collection of recombinant cell clones obtainable by this method and kit for screening comprising said collection.

The invention is also directed to a yeast or bacterial two-hybrid system method for identifying a recombinant cell clone expressing a prey polypeptide of a prokaryotic microorganism capable of interacting with a bait polypeptide and a method for identifying said prey polypeptide.

The present invention further comprises polynucleotides or polypeptides corresponding to the prey polypeptides capable of interacting with a bait polypeptide and the protein-protein interactions identified by the yeast or bacterial two-hybrid system method according to the invention, vectors and host cells containing said polynucleotides, and pharmaceutical composition including them.

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The present invention also concerns a method for identifying a polynucleotide encoding a selected interacting domain (SID®) of a prey polypeptide of interest from a prokaryotic microorganism capable of interacting with a bait polypeptide.

Another aspect of the present invention relates to a method for selecting an agent capable of modulating the protein-protein interaction identified by the yeast or bacterial two-hybrid system method according to the invention.

Brief description of the drawings

Figure 1 is a restriction map of the plasmid pAS2ΔΔ which may be used for the veast two-hybrid system.

Figure 2 is a restriction map of the plasmid pACTIIst which may be used for the yeast two-hybrid system.

Figure 3 is a restriction map of the plasmid pUT18 which may be used for the bacterial two-hybrid system. In this figure, each multicloning site (MCS) is detailled.

Figure 4 is a restriction map of the plasmid pUT18C which may be used for the bacterial two-hybrid system. In this figure, each multicloning site (MCS) is detailled.

Figure 5 is a restriction map of the plasmid pT25 which may be used for the bacterial two-hybrid system. In this figure, each multicloning site (MCS) is detailled.

Figure 6 is a restriction map of the plasmid pKT25 which may be used for the bacterial two-hybrid system. In this figure, each multicloning site (MCS) is detailled.

Figure 7 is a schematic representation of the SID® identification method. In this figure, the « Full-length prey protein » is the Open Reading Frame where the identified prey polypeptides are included, the Selected Interaction Domain SID® is determined by comparison of every prey polypeptide fragment.

Figure 8 is a restriction map of the plasmid pP6 which may be used for the yeast two-hybrid system.

Detailed description of the invention

The present invention is directed to a method for producing a collection of recombinant cell clones usable for two-hybrid systems comprising the steps of:

a) fragmenting DNA;

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- b) inserting polynucleotidic fragments obtained in step a) in plasmids in such a way that the expression of said plasmids in host cell leads to an hybrid polypeptide containing a specific domain capable of activating a reporter gene when associated with a complementary domain;
- 5 c) transforming cell clones with plasmids obtained in step b); and
 - d) optionally, selecting the transformed recombinant cell clones obtained in step c); wherein DNA of step a) is genomic DNA obtained from a prokaryotic micro-organism.

The step a) of fragmenting DNA according to the method of the invention may be obtained by enzyme digestion, sonication or nebulization of the source of genomic DNA, sonication and nebulization ensuring a random cleavage of the starting DNA material and thus an excellent representation of all the possible inserts.

In a preferred embodiment, the step a) of fragmenting DNA of the method according to the invention is carried out by a nebulization process, for example, with a commercial nebulizer (GATC).

In a preferred embodiment, the plasmid used in the method for producing a collection of recombinant cell clones usable for two-hybrid systems according to the present invention may comprise in addition a nucleic sequence encoding a promoter, a multicloning site, a terminator site and a selection marker, operably linked.

A "promoter" refers to a DNA sequence recognized by the transcriptional machinery of the cell required to initiate the specific transcription of a gene.

A sequence which is "operably linked" to a regulatory sequence such as a promoter means that said regulatory element is in the correct location and orientation in relation to the nucleic acid to control RNA polymerase initiation and expression of the nucleic acid of interest. As used herein, the term "operably linked" refers to a linkage of polynucleotide elements in a functional relationship. For instance, a promoter or enhancer is operably linked to a coding sequence if it affects the transcription of the coding sequence. More precisely, two DNA molecules (such as a polynucleotide containing a promoter region and a polynucleotide encoding a desired polypeptide or polynucleotide) are said to be "operably linked" if the nature of the linkage between the two polynucleotides does not (1) result in the introduction of a frame-shift mutation or (2) interfere with the ability of the polynucleotide containing the promoter to direct the transcription of the coding polynucleotide.

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As a promoter, one could use full or truncated ADH promoter.

By specific domain, it is intended a domain whose association with a complementary domain leads to the activation of a reporter gene.

In one particular embodiment of this invention, the specific domain may be a transcriptional activating domain or a DNA-binding domain and the complementary domain may, respectively, be a DNA binding domain or a transcriptional activation domain.

Transcriptional activating domain and DNA-binding domain may be derived from Gal4 and LexA respectively.

In another particular embodiment of the invention, the activation domain is a part of an enzyme and the complementary domain is the other part of the same enzyme. Proximity of the two parts of the enzyme may restore the enzyme activity and activate a reporter gene.

For example, specific and complementary domain may be T25 and T18 polypeptides that constitute the catalytic domain of *Bordetella pertussis* adenylate cyclase.

The reporter gene may be contained either in a plasmid of recombinant cell clone or in its genome.

As an illustrative embodiment of the invention, the reporter gene is chosen among the group consisting in a nutritional gene or also a gene the expression of which is visualized by colorimetry such as His3, LacZ or both LacZ and His3.

As a selective marker, gene encoding for a toxin, color marker of the type of the Green Fluorescent Protein (GFP), gene encoding for phage receptor proteins or fragment thereof such as phage λ receptor lam B and any other gene giving selectable phenotype, resistance gene, such as ampicilline, kanamycin, tetracyclin or lactose or maltose nutritional gene, may be used.

In a particularly preferred embodiment, the invention relates to a method according to the invention wherein DNA of step a) is genomic DNA obtained from *Helicobacter pylori* (see example 1.A.), *Escherichia coli*, *Staphylococcus aureus* and *Streptococcus pneumoniae*.

The invention also concerns a collection of recombinant cell clones usable for two-hybrid systems obtainable by a method according to the invention.

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The invention further concerns a collection of recombinant cell clones usable for two-hybrid systems, each recombinant cell clone containing a polynucleotide inserted in a plasmid whose expression leads to hybrid polypeptide containing a specific domain, wherein the said polynucleotide is a genomic DNA fragment obtained from a prokaryotic micro-organism.

In a preferred embodiment, said genomic DNA fragment is obtained by a fragmentation process by nebulization.

In a particularly preferred embodiment, the invention relates to collection of recombinant cell clones of the invention wherein the prokaryotic micro-organism is Helicobacter pylori, Escherichia coli, Staphylococcus aureus and Streptococcus pneumoniae.

The present invention also comprises a collection of recombinant cell clones according to the invention, wherein the recombinant cell clones are selected from the group consisting of Gram+ or Gram- bacteria, yeasts, fungi and mammalian cells, particularly from the group consisting of *Escherichia coli* bacteria and *Saccharomyces cerevisiae* yeast.

The present invention further concerns a collection of recombinant cell clones according to the invention, wherein the plasmids comprise at least a nucleic sequence coding a promoter, a specific domain, a multicloning site where the said polypeptide is cloned, and a selection marker.

In a preferred embodiment, the present invention further concerns a collection of recombinant cell clones according to the invention, wherein the polynucleotide is inserted in the plasmid pACTIIst or in the plasmid pP6.

In a more preferred embodiment, the present invention further concerns a collection of recombinant cell clones according to the invention, wherein the collection contains 10^6 to 10^7 or to 10^8 recombinant *Escherichia coli* clones and wherein the proportion of independent cell clones with insert is at least 60 %, 70 %, 80 %, 90 %, 95 % or 97 %.

The present invention particularly comprises the collection of recombinant cell clones according to the invention which has been deposited in the Collection National de Cultures de Microorganismes (CNCM) (France, Paris) on April 13, 1999 under the

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accession number I-2181, and on March 23, 2000 under the accession numbers I-2416, I-2414, I-2415 and I-2417.

The collection of recombinant cell clones which has been deposited under the accession number I-2181 (identification reference: HGXBHP1) concerns a genomic librairy of *Helicobacter pylori* 26695 strain, cloned in the stop bis pACTII vector, transformed in *Escherichia coli* DH10B. The collection contains about 10⁷ independent clones with an insert pourcentage of about 97 % and an insert average size of 1000 pb.

The collection of recombinant cell clones which has been deposited under the accession number I-2416 (identification reference: HGXBSA1) concerns a genomic librairy of *Staphylococcus aureus* col strain, cloned in the pP6 vector, transformed in *Escherichia coli* DH10B. The collection contains about 6.8 10⁷ independent clones with an insert pourcentage superior to 95 % and an insert average size of 1100 pb.

The collection of recombinant cell clones which has been deposited under the accession number I-2415 (identification reference: HGXBEC1) concerns a genomic librairy of *Escherichia coli* MG1655 strain, cloned in the pP6 vector, transformed in *Escherichia coli* DH10B. The collection contains about 3 10⁷ independent clones with an insert pourcentage superior to 98 % and an insert average size of 853 pb.

The collection of recombinant cell clones which has been deposited under the accession number I-2417 (identification reference: HGXBHP4) concerns a genomic librairy of *Helicobacter pylori* 26695 strain, cloned in the pP6 vector, transformed in *Escherichia coli* DH10B. The collection contains about 1.9 10⁷ independent clones with an insert pourcentage superior to 98 % and an insert average size of 1009 pb.

In another aspect, the present invention relates to a collection of recombinant cell clones according to the invention, wherein the collection contains 10^5 to 1.5×10^7 haploid recombinant *Saccharomyces cerevisiae* clones and wherein the proportion of independant cell clones with insert is at least 60 %, 70 %, 80 %, 90 %, 95 % or 97 %.

The present invention particularly comprises the collection of recombinant cell clones according to the invention which has been deposited in the Collection National de Cultures de Microorganismes (CNCM) on April 13, 1999 under the accession

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number I-2182, and on March 23, 2000 under the accession numbers I-2420, I-2419 and I-2418.

The collection of recombinant cell clones which has been deposited under the accession number I-2182 (identification reference: HGXYHP1) concerns a genomic librairy of *Helicobacter pylori*, 26195 strain, which has been amplified in *E. coli* (HGXBHP1 librairy), cloned in the stop bis pACTII vector, transformed in *Saccharomyces cerevisiae*, Y187 strain, and containing about 2 10⁶ independent clones.

The collection of recombinant cell clones which has been deposited under the accession number I-2420 (identification reference: Lib Sa2) concerns a genomic librairy of *Staphylococcus aureus*, col strain, which has been amplified in *E. coli* (HGXBSA1 librairy), cloned in the pP6 vector, transformed in *Saccharomyces cerevisiae*, Y187 strain, containing about 2.2 10⁶ independent clones, and a cell concentration about 5 10⁸ cells/ml.

The collection of recombinant cell clones which has been deposited under the accession number I-2419 (identification reference: Sp in Y187 pP6) concerns a genomic librairy of *Streptococcus pneumoniae*, type 4 strain, which has been amplified in *E. coli* (HGXBSP1 librairy), cloned in the pP6 vector, transformed in *Saccharomyces cerevisiae*, Y187 strain, containing about 2.8 10⁶ independent clones, and a cell concentration about 5 10⁸ cells/ml.

The collection of recombinant cell clones which has been deposited under the accession number I-2418 (identification reference: E.coli in Y187 lib1) concerns a genomic librairy of Escherichia coli, MG1655 strain, which has been amplified in E. coli (HGXBEC1 librairy), cloned in the pP6 vector, transformed in Saccharomyces cerevisiae, Y187 strain, containing about 4 10⁶ independent clones, and a cell concentration about 5 10⁸ cells/ml.

In another aspect, the present invention relates to a collection of recombinant cell clones according to the invention, wherein the polynucleotide is inserted in the plasmid $pAS2\Delta\Delta$.

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Still another aspect, the present invention relates to a collection of recombinant cell clones according to the invention, wherein the polynucleotide is inserted in a plasmid selected from the group consisting of pT25, pKT25, pUT18 and pUT18C.

The present invention also relates to a kit for screening protein-protein interaction comprising a collection of recombinant cell clones usable for two-hybrid systems according to the invention.

In a particular embodiment of the collection according to the invention, the DNA library is presented as a ready to use kit for screening protein-protein interaction consisting in a collection of recombinant haploid yeast cells containing the whole genome as inserts generated during the construction of the DNA library under the form of prey polynucleotides, said collection of yeast cells being frozen in multiple vial containing an identical biological material.

The present invention also provides a generally method for selecting a polynucleotide of the collection according to the present invention, encoding a prey polypeptide, that is capable of interacting with bait polypeptide of interest.

As used interchangeably herein, the terms "polynucleotides", "nucleic acid" "oligonucleotides", include RNA, DNA, or RNA/DNA hybrid sequences of more than one nucleotide in either single chain or duplex form. The polynucleotide sequences of the invention may be prepared by any known method, including synthetic, recombinant, ex vivo generation, or a combination thereof, as well as utilizing any purification methods known in the art.

The term "purified" is used herein to describe a polynucleotide of the invention which has been separated from other compounds including, but not limited to other nucleic acids, carbohydrates, lipids and proteins. A polynucleotide is substantially pure when at least about 50 %, preferably 60 to 90 % weight/weight of a sample exhibits a single polynucleotide sequence, more usually about 95 %, and preferably is over about 99 %.

As used herein, the term "isolated" requires that the material be removed from its original environment (e.g., the natural environment if it is naturally occurring). For example, a naturally-occurring polynucleotide or polypeptide present in a living animal is not isolated, but the same polynucleotide or DNA or polypeptide, separated from some or all of the coexisting materials in the natural system, is isolated. Such

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polynucleotide could be part of a vector and/or such polynucleotide or polypeptide could be part of a composition, and still be isolated in that the vector or composition is not part of its natural environment.

The term "polypeptide" refers to a polymer of amino acids without regard to the length of the polymer; thus, peptides, oligopeptides, and proteins are included within the definition of polypeptide, theses terms as used herein are interchangeable. The term "polypeptide" also does not specify or exclude post-expression modifications of polypeptides, for example, polypeptides which include the covalent attachment of glycosyl groups, acetyl groups, phosphate groups, lipid groups and the like are expressly encompassed by the term polypeptide. Also included within the definition are polypeptides which contain one or more analogs of an amino acid (including, for example, non-naturally occurring amino acids, amino acids which only occur naturally in an unrelated biological system, modified amino acids from mammalian).

The term "purified" is used herein to describe a polypeptide of the invention which has been separated from other compounds including, but not limited to nucleic acids, carbohydrates, lipids and other proteins. A purified polypeptide typically comprises about 50 %, preferably 60 to 90 % weight/weight of a protein sample, more usually about 95 %, and preferably is over about 99 % pure.

Bait polypeptide of interest is either a prokaryotic polypeptide encoded by a polynucleotide of the collection according to the present invention, or any other polypeptides of interest. Other polypeptides of interest can be polypeptides of an organism that may be infected by the prokaryotic micro-organism, for example, mammalian organism, in particular human organism.

The following described method is the mating yeast two-hybrid system and the bacterial two-hybrid system but variants of two-hybrid systems could also be used.

For example, the three hybrid system (Tirode et al., 1997, Journal of Biological Chemistry, 272, 22995-22999, A conditionally expressed third partner stabilises or prevents the formation of a transcriptional activator in a three-hybrid system) involves three polypeptides that allow or prevent the formation of the transcriptional activator. Beside the two-hybrid fusion proteins, the third partner is under the control of the Met25 promoter, which is positively regulated in medium lacking methionine. Another variant is the reverse two-hybrid system (Vidal et al., 1996, Proc. Natl. Sci., 93, 10315-

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10320, Reverse two-hybrid and one-hybrid system to detect dissociation of protein-protein and DNA-protein interaction) where a collection of molecules can be screened that may inhibit a specific protein-protein interaction.

Yet another aspect, the present invention relates to yeast two-hybrid system method for identifying a recombinant cell clone containing a prey polynucleotide encoding a prey polypeptide capable of interacting with a bait polypeptide comprising the steps of:

- a) mating at least one first haploid recombinant cell clone of a collection of recombinant cell clones according to the invention transformed with a plasmid containing the prey polynucleotide to be assayed with a second haploid recombinant S. cerevisiae cell clone transformed with a plasmid containing a bait polynucleotide encoding said bait polypeptide;
- b) cultivating diploid cell obtained in step a) on selective medium; and
- c) selecting recombinant cell clones capable of growing on selective medium.

In a particular embodiment, the invention is directed to a yeast two-hybrid system method for identifying a prey polynucleotide encoding a prey polypeptide capable of interacting with a bait polypeptide comprising the steps of:

- a) identifying a recombinant cell clone containing a prey polynucleotide encoding a
 prey polypeptide capable of interacting with a bait polypeptide according to the
 invention; and
- b) characterizing the prey polynucleotide contained in each recombinant cell clone selected in step a).

By yeast two-hybrid system is intended a method that usually makes use of at least one reporter gene, the transcription of which is activated when a prey polypeptide and a bait polypeptide produced by recombinant cell, due to the triggering of the transcription of said at least one reporter gene when both the specific domain contained in one prey polypeptide and the complementary domain contained in the bait polypeptide are in proximity one to the other. In an advantageous variant of yeast two hybrid system, prey polynucleotides encoding for prey polypeptides and bait polynucleotides encoding for bait polypeptides or proteins are inserted in recombinant haploid yeast cells, then a mating step leads to diploid yeast cells that produce the prey polypeptide and the bait polypeptide.

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By at least one reporter gene according to the invention, it is intended from one to five, and preferably two or three reporter genes, the transcription of which is activated within the recombinant diploid yeast cell when the encoded bait and prey polypeptide are capable of interacting.

Preferably, the at least one reporter gene is contained in the first recombinant haploid yeast cell containing the bait polynucleotide.

The at least one reporter gene may be contained either in a plasmid of the recombinant diploid yeast cell or in its genome.

As an illustrative embodiment, the at least one reporter gene is located in the chromosome of one recombinant haploid yeast cell used according to the previously described two-hybrid system and preferably the yeast cell containing the bait polynucleotide. The at least one reporter gene can be chosen among the group consisting in a nutritional gene or also a gene the expression of which is visualized by colorimetry, such as His3, LacZ or both LacZ and His3.

By "prey polynucleotide", it is intended a chimeric polynucleotide encoding a chimeric polypeptide comprising i) a specific domain and ii) a polypeptide that is to be tested for interaction with a bait polypeptide. The specific domain is preferably a transcriptional activating domain.

The prey polynucleotide may be obtained from a genomic library of a prokaryotic micro-organism, preferably from genomic DNA of *Helicobacter pylori*.

By a "bait polynucleotide", it is intended a chimeric polynucleotide encoding a chimeric polypeptide comprising i) a complementary domain and ii) a polypeptide that is to be tested for interaction with at least one prey polypeptide. The complementary domain is preferably a DNA-binding domain that recognizes a binding site on a detectable gene that is contained in a host organism.

Using as the bait polynucleotide, a complete open reading frame (ORF) that may be obtained either by digestion with a restriction endonuclease (Sambrook et al., 1973, Biochemistry 12(16): 3055-63 Detection of two restriction endonuclease activities in Haemophilus parainfluenzae using analytical agarose-ethidium bromide electrophoresis) or by digestion with an exonuclease such as Ball, or also by DNA synthesis. The complete ORF can also correspond to a given prey selected at given round with a two-hybrid system. An "open reading frame", also referred to herein as

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ORF, is a region of nucleic acid which encodes a polypeptide. This region may represent a portion of a coding sequence or a total sequence and be determined from a stop to stop codon or from a start to stop codon.

"DNA-binding domain" refers to a protein that specifically interacts with desoxyribonucleotide strands. A sequence-specific DNA binding protein binds to a specific sequence or family of specific sequences showing a high degree of sequence identity with each other.

The DNA binding domain of the bait polypeptide and the transcriptional activating domain of the prey polypeptide may be of different kinds. As an illustrative embodiment, these can be derived from LexA or also Gal4.

In one particular experiment of the yeast two-hybrid system, prey polypeptides are encoded by prey polynucleotides cloned in plasmid pACTIIst carrying Leu2 selection gene transformed in Y187 yeast cells carrying leucine auxotrophy and bait polypeptide are encoded by bait polynucleotide cloned in plasmid pAS2ΔΔ carrying Trp1 selection gene transformed in CG1945 yeast cells carrying tryptophane auxotrophy.

In another aspect, the present invention relates to a bacterial two-hybrid system method for identifying a recombinant cell clone containing a prey polynucleotide encoding a prey polypeptide capable of interacting with a bait polypeptide comprising the steps of:

- a) transforming bacterial cell clones with a plasmid containing a bait polynucleotide encoding said bait polypeptide;
- b) rescuing prey plasmids containing prey polynucleotides from the collection according to the present invention;
- c) transforming the recombinant bacterial cell clones obtained in step a) with the plasmid rescued in step b);
 - d) cultivating bacterial recombinant cells obtained in step c) on selective medium;
 - e) selecting recombinant cell clones capable of growing on selective medium.c) selecting recombinant cell clones capable of growing on selective medium.

In a preferred embodiment, the preparation of bacterial recombinant cells obtained in step c) of the bacterial two-hybrid system method for identifying a recombinant cell clone according to the invention comprises the following steps:

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- 1) E. coli is firstly transformed with bait plamid (standard protocol with chimio- or electro-competent cells);
- 2) prey plasmids are rescued from collection according to the invention (prey plasmids are in *E. coli* bacterial strain, cf. protocol 1.B « the plasmid DNA contained in E. coli are extracted (Qiagen) from aloquoted E. coli frozen cells »);
- 3) rescued prey plasmids are then transformed in recombinant *E coli* of step 1 according to standard protocols of transformation (for example using electro- of chimio-competent cells).

In a particular embodiment, the invention is directed to a bacterial two-hybrid system method for identifying a prey polynucleotide encoding a prey polypeptide capable of interacting with a bait polypeptide comprising the steps of:

- a) identifying a recombinant cell clone containing a prey polynucleotide encoding a prey polypeptide capable of interacting with a bait polypeptide according to the invention; and
- b) characterizing the prey polynucleotide contained in each recombinant cell clone selected in step a).

By bacterial two-hybrid system is intended a method that usually makes use of at least one reporter gene, the transcription of which is activated when a prey polypeptide and a bait polypeptide produced by recombinant cell, due to the triggering of the transcription of said at least one reporter gene when both the specific domain contained in one prey polypeptide and the complementary domain contained in the bait polypeptide are in proximity one to the other.

In a particular embodiment of the bacterial two-hybrid system, specific domain of prey polypeptide and complementary domain of bait polypeptide are part of the catalytic domain of an enzyme. Interaction of prey polypeptide and bait polypeptide allows restoration of enzyme catalytic domain and, as a consequence, to the restoration of the enzyme activity.

In a more preferred embodiment of the bacterial two-hybrid method, enzyme is Bordetella *pertussis* adenylate cyclase which activation, via proximity of T25 and T18 fragments of the catabolic domain, leads to cAMP synthesis, cAMP then triggers transcriptional activation of catabolic operons, such as lactose or maltose.

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Still another aspect, the present invention relates to a method according to the invention, wherein the bait polypeptide and the prey polypeptide (encoded by a polynucleotide inserted in cell clone from the collection according to the present invention) are originating from the same prokaryotic micro-organism, particularly from Helicobacter pylori, Escherichia coli, Staphylococcus aureus or Streptococcus pneumoniae or wherein the bait polypeptide is originating from a human polypeptide and the prey polypeptide is originating from a prokaryotic micro-organism, particularly from Helicobacter pylori.

Yet another aspect, the present invention relates to a recombinant diploid yeast cell obtained by step a) of the yeast two-hybrid system method for identifying a recombinant cell clone according to the invention as described above.

The recombinant diploid yeast cell obtained by the the yeast two-hybrid system method for identifying a recombinant cell clone according to the invention, also forms part of the present invention.

By performing yeast or bacterial two-hybrid system, it can be possible to identify for one particular bait interacting prey polypeptide. Prey polynucleotide that has been selected by testing the collection in a screening two-hybrid method encodes for polypeptide interacting with a protein of interest.

The running of the two-hybrid method leads to the identification of interactions between prokaryotic prokaryotic polypeptides, especially *Helicobacter pylori*, *Escherichia coli*, *Staphylococcus aureus* or *Streptococcus pneumoniae* polypeptides, or eukaryotic-prokaryotic polypeptides, these interactions are also part of the invention.

In another aspect, the present invention is directed to a polynucleotide, or fragment thereof, encoding a prey polypeptide capable of interacting with a bait polypeptide wherein said polynucleotide is identified by a method according to the invention.

In a preferred embodiment, the invention comprises the polynucleotides according to the invention, selected from the group consisting of:

a) a polynucleotide having the nucleic acid sequence of an ORF identified by the reference indicated in the right column "interacting ORF" in table I, and fragment thereof having at least 12 consecutive nucleotides;

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- b) a polynucleotide having at least 80 %, preferably at least 85 %, 90 %, 95 % and 99 %, nucleotides identity degree after alignment to a nucleic acid sequence of a polynucleotide of a);
- c) a polynucleotide comprising the nucleic acid sequence of a polynucleotide of a) or b).

Still another aspect, the present invention is directed to a polynucleotide, or fragment thereof, encoding a bait polypeptide capable of interacting with a prey polypeptide wherein the polynucleotide encoding said prey polypeptide is identified by a method according to the invention.

In a preferred embodiment, the invention comprises the polynucleotides according to the invention, selected from the group consisting of:

- a) a polynucleotide having the nucleic acid sequence of an ORF identified by the reference indicated in the left column "bait polypeptide" in table I, and fragment thereof having at least 12 consecutive nucleotides;
- b) a polynucleotide having at least 80 %, preferably at least 85 %, 90 %, 95 % and 99 %, identity degree after alignment to a nucleic acid sequence of a polynucleotide of a);
 - c) a polynucleotide comprising the nucleic acid sequence of a polynucleotide of a) or b).

Yet another aspect, the present invention relates to a set of two polynucleotides consisting of a first polynucleotide, or fragment thereof, encoding a prey polypeptide capable of interacting with a bait polypeptide according to the invention and a second polynucleotide, or a fragment thereof having at least 12 consecutive nucleotides, encoding said bait polypeptide.

The polypeptides encoded by the polynucleotides according to the invention and the sets of two polypeptides encoded by the sets of two polynucleotides according to the invention, also form part of the invention.

In a preferred embodiment, the invention concerns an isolated complex comprising at least the two polypeptides encoded by a set of two polynucleotides according to the invention, preferably said two polypeptides are associated in the complex by affinity binding.

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In a preferred embodiment, the invention concerns an isolated complex comprising at least a polypeptide encoded by the ORF HP1198 (or a fragment thereof, preferably one of its SID® domains, or homologuous polypeptide thereof exhibiting at least 80 % identity degree) and a polypeptide encoded by the ORF HP1293 (or a fragment thereof, preferably one of its SID® domains, or homologuous polypeptide thereof exhibiting at least 80 % identity degree).

In a preferred embodiment, the invention concerns an isolated complex comprising at least a polypeptide encoded by the ORF HP1198 (or a fragment thereof, preferably one of its SID® domains, or homologuous polypeptide thereof exhibiting at least 80 % identity degree) and a polypeptide encoded by the ORF HP0088 (or a fragment thereof, preferably one of its SID® domains, or homologuous polypeptide thereof exhibiting at least 80 % identity degree).

In a preferred embodiment, the invention concerns an isolated complex comprising at least a polypeptide encoded by the ORF HP1198 (or a fragment thereof, preferably one of its SID® domains, or homologuous polypeptide thereof exhibiting at least 80 % identity degree) and a polypeptide encoded by the ORF HP1032 (or a fragment thereof, preferably one of its SID® domains, or homologuous polypeptide thereof exhibiting at least 80 % identity degree).

In another aspect, the present invention relates to a protein-protein interaction wherein the two interacting proteins consist of a set of two polypeptides according to the invention.

In a preferred embodiment, the invention relates to the protein-protein interactions according to the invention, wherein the sets of two polypeptides consist of two Helicobacter pylori, Escherichia coli, Staphylococcus aureus or Streptococcus pneumoniae polypeptides.

When several reiterations of the two-hybrid method are performed and thus common bait and prey polypeptide are selected, a map of all the interactions between these polypeptides may be designed, that take into account of the known and/or suspected biological function of each of the interacting polypeptides.

Such an Proteins Interaction Map (PIM®) may help the one skilled in the art to decipher a whole metabolical and/or physiological pathway that is functionally active

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within the host organism from which the initial DNA library is derived. Protein Interaction Map and computable version of PIM® are part of the present invention.

Therefore still another aspect, the present invention is directed to a computable readable medium (such as floppy disk, diskette, CD-rom, and all electronic or magnetic format which can be read by a computer) having stored thereon protein-protein interactions according to the invention, preferably stored in a form of a protein interaction map, as showed, for example, in Fromont-Racine et al., Nature Genetics, 1997, Letter, 277-281, figure 3, page 279.

In a preferred embodiment, the invention comprises a computable readable medium according to the invention, wherein the protein-protein interactions stored thereon are linked to annotated database, for example through Internet.

In an other preferred embodiment, the invention comprises a data bank containing the protein-protein interactions stored thereon, said databank being avalaible on a World-Wide Web site, said databank may be annoted by means of others databank.

As the source genomic DNA is randomly fragmented before being inserted in recombinant vectors, several prey polypeptides may be selected for one bait polypeptide. Therefore it is possible to define the Selected Interacting Domain (SID®) which contains the precise polypeptide domain involved in the interaction between the prey polypeptide and the bait polypeptide.

So, in another aspect, the invention relates to a method for identifying a polynucleotide encoding a selected interacting domain (SID®) of a prey polypeptide of interest from a prokaryotic micro-organism capable of interacting with a bait polypeptide comprising the steps of:

- a) selecting from prey polynucleotides identifying by a method according to the invention all prey polynucleotides encoding a polypeptide capable of interacting with said bait polypeptide and containing a nucleic acid fragment identical to a nucleic fragment of the polynucleotide encoding the prey polypeptide of interest;
- b) determining the polynucleotide common to said all prey polynucleotides selected in step a); and
- c) identifying the polynucleotide determining in step b) as being the polynucleotide encoding the selected interacting domain (SID®) of said prey polypeptide of interest.

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The polynucleotides encoding a selected interacting domain (SID®) of a prey polypeptide of interest from a prokaryotic micro-organism capable of interacting with a bait polypeptide obtainable by this method, also form part of the invention.

In a particular embodiment, the prey polypeptide of interest is originating from Helicobacter pylori, Escherichia coli, Staphylococcus aureus or Streptococcus pneumoniae.

In a preferred embodiment, the polynucleotides encoding a selected interacting domain (SID®) of a prey polypeptide of interest according to the invention are selected from the group consisting of:

- a) a polynucleotide encoding an amino acids sequence identified by the reference indicated in the right column "SID®" in table II;
 - b) a polynucleotide having the sequence identified by the reference indicated in the right column "SID®" in table III;
 - c) fragment having at least 12, 15, 25 or 50 consecutive nucleotides of polynucleotide of a) or b), complement thereof, and RNA corresponding to said polynucleotide; and
 - d) a polynucleotide having at least 80 %, preferably 85 %, 90 %, 95 % and 99 %, identity degree after alignment to a nucleic acid sequence of a polynucleotide of a) or b).

The term "complement thereof" are used herein to refer to the sequences of polynucleotides which is capable of forming Watson & Crick base pairing with another specified polynucleotide throughout the entirety of the complementary region. This term is applied to pairs of polynucleotides based solely upon their sequences and not any particular set of conditions under which the two polynucleotides would actually bind.

The term "degree of sequence identity" is used herein to refer to comparisons among polynucleotides and polypeptides, and are determined by comparing two optimally aligned sequences over a comparison window, wherein the portion of the polynucleotide or polypeptide sequence in the comparison window may comprise additions or deletions (i.e., gaps) as compared to the reference sequence (which does not comprise additions or deletions) for optimal alignment of the two sequences. The percentage is calculated by determining the number of positions at which the identical nucleic acid base or amino acid residue occurs in both sequences to yield the number of matched positions, dividing the number of matched positions by the total number of

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positions in the window of comparison and multiplying the result by 100 to yield the percentage of sequence identity. Homology is evaluated using any of the variety of sequence comparison algorithms and programs known in the art. Such algorithms and programs include, but are by no means limited to BLASTN, BLASTP (Altschul et al., 1990, J. Mol. Biol. 215(3): 403-410 / Altschul et al., 1993, Nature Genetics 3:266-272 / Altschul et al., 1997, Nuc. Acids Res. 25:3389-3402).

The definition of sequence identity given above is the definition that would use one of skill in the art. The definition by itself does not need the help of any algorithm, said algorithms being helpful only to achieve the optimal alignments of sequences, rather than the calculation of sequence identity.

From the definition given above, it follows that there is a well defined and only one value for the sequence identity between two compared sequences which value corresponds to the value obtained for the best or optimal alignement.

In the BLAST N or BLAST P "BLAST 2 sequence" (Tatusova et al., Blast 2 sequences - a new tool for comparing protein and nucleotide sequences, FEMS Microbiol. Lett. 174: 247-250) software which is available in the web site http://www.ncbi.nlm.nih.gov/gorf/bl2.html, and habitually used by the inventors and in general by the skilled man for comparing and determining the identity between two sequences, the "open gap penaltie" and « extension gap penaltie » parameters which depend on the substitution matrix selected regarding the nature and the length of the sequence to be compared are directly selected by the software (i.e "5" and "2" respectively for substitution matrix BLOSUM-62). The identity percentage between the two sequences to be compared is directly calculated by the software.

In another object, the invention also comprises the polypeptides selected from the group consisting of:

- a) a polypeptide having an amino acids sequence identified by the reference indicated in the right column "SID®" in table II, and fragment thereof having at least 5 consecutive amino acids; and
- b) a polypeptide encoded by a polynucleotide encoding a selected interacting domain (SID®) of a prey polypeptide of interest according to the invention.

Still another aspect, the invention relates to the use of a polynucleotide according to the present invention as a primer or a probe for the amplification and/or the

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detection of polynucleotide encoded a prey polypeptide of interest, or its SID®, capable of interacting with a bait polypeptide according to the present invention.

In another aspect, the present invention concerns cloning or expression vector containing a polynucleotide according to the invention.

Particularly preferred vectors of the invention include the plasmid pACTIIst, pAS2 $\Delta\Delta$, pP6 or the plasmid selected from the group consisting of pT25, pKT25, pUT18 and pUT18C.

Further preferred vectors are self replicated or viral vectors, such as adenovirus, AAV, a retrovirus, a poxvirus or an herpes virus.

The vectors according to the invention, characterized in that they comprise the elements allowing the expression and/or the secretion of the said sequences in a host cell, also form part of the invention.

Vector according to the invention including elements allowing expression and/or secretion of said polynucleotide in a host cell also form part of the invention.

The vectors according to the invention characterized in that they comprise a promoter and/or regulator sequence, or a sequence for cellular addressing according to the invention, or one of their fragments, are also included in the invention.

The said vectors will preferably comprise a promoter, signals for initiation and termination of translation, as well as appropriate regions for regulation of transcription. They may also be capable of being stably maintained in the cell and may optionally possess particular signals specifying the secretion of the translated protein.

These different control signals are chosen according to the cellular host used. To this end, the nucleic acid sequences according to the invention may be inserted into autonomously replicating vectors inside the chosen host, or integrative vectors of the chosen host.

Among the autonomously or self replicating systems, there will be preferably used according to the host cell, systems of the plasmid or viral type, it being possible for the viral vectors to be in particular adenoviruses (Perricaudet et al., 1992, La Recherche 23: 471-473, 1992), retroviruses, poxviruses or herpes viruses (Epstein et al., 1992, Médecine/Sciences 8: 902-911, 1992). Persons skilled in the art know the technologies which can be used for each of these systems.

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When the integration of the sequence into the chromosomes of the host cell is desired, it will be possible to use, for example, systems of the plasmid or viral type; such viruses will be, for example, retroviruses (Temin, 1986, In Kucherlapati R., ed. Gene Transfer, New York, Plenum Press, 149-187, 1986), or AAVs (Carter, 1993, Curr. Op. Biotechnology 3: 533-539, 1993).

Such vectors will be prepared according to the methods commonly used by persons skilled in the art, and the clones resulting therefrom may be introduced into an appropriate host by standard methods such as, for example, lipofection, electroporation or heat shock.

The invention comprises, in addition, the host cells, in particular eukaryotic and prokaryotic cells, transformed by the vectors according to the invention.

Among the cells which can be used for these purposes, there may of course be mentioned bacterial cells (Olins et al., Curr. Op. Biotechnology 4: 520-525, 1993), but also yeast cells (Buckholz, Curr. Op. Biotechnology 4: 538-542, 1993), as well as animal cells, in particular mammalian cell cultures (Edwards and Aruffo, Curr. Op. Biotechnology 4: 558-563, 1993), and in particular Chinese hamster ovary cells (CHO), but also insect cells in which it is possible to use methods using baculoviruses, for example (Luckow et al., Curr. Op. Biotechnology 4: 564-572, 1993). A preferred cellular host for the expression of the proteins of the invention consists of the CHO cells.

The cells according to the invention can be used in a method for the production of a polypeptide according to the invention, as described below, and can also serve as a model for analysis and screening.

So, the present invention comprises a method for producing a polypeptide of the invention comprising the steps of:

- a) cultivating a host cell according to the invention under conditions and in culture medium allowing the growth of said host cell and the expression of said polypeptide; and
- b) recovering said polypeptide directly from the culture medium or from said cultivated cell obtained in step a).

Recombinant polypeptide obtained by the method above also form part of the invention.

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The term "recombinant polypeptide" is used herein to refer to polypeptides that have been artificially designed and which comprise at least two polypeptide sequences that are not found as contiguous polypeptide sequences in their initial natural environment, or to refer to polypeptides which have been expressed from a recombinant polynucleotide.

The method for the production of a polypeptide of the invention in recombinant form is itself included in the present invention, and is characterized in that the transformed cells, are cultured under conditions allowing the expression of a recombinant polypeptide encoded by a polynucleotide according to the invention, and in that the said recombinant polypeptide is recovered.

Also forming part of the invention is a method for the production of a heterologous polypeptide, characterized in that it uses a vector or a host cell according to the invention.

The recombinant polypeptides, characterized in that they are obtainable by the said method of production, also form part of the invention.

The recombinant polypeptides obtained as indicated above may be both in glycosylated and non-glycosylated form and may or may not have the natural tertiary structure.

These polypeptides may be produced from the polynucleotide, according to techniques for the production of recombinant polypeptides known to persons skilled in the art. In this case, the polynucleotide used is placed under the control of signals allowing its expression in a cellular host.

An effective system of production of a recombinant polypeptide requires having a vector and a host cell according to the invention.

These cells may be obtained by introducing into the host cells a nucleotide sequence inserted into a vector as defined above, and then culturing the said cells under conditions allowing the replication and/or expression of the transfected nucleotide sequence.

The methods for the purification of a recombinant polypeptide which are used are known to persons skilled in the art. The recombinant polypeptide may be purified from cell lysates and extracts, from the culture medium supernatant, by methods used individually or in combination, such as fractionation, chromatographic methods,

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immunoaffinity techniques with the aid of specific mono- or polyclonal antibodies, and the like.

A preferred variant consists in producing a recombinant polypeptide fused with a "carrier" protein (chimeric protein). The advantage of this system is that it allows a stabilization and a reduction in proteolysis of the recombinant product, an increase in solubility during in vitro renaturation and/or simplification of the purification when the fusion partner has affinity for a specific ligand.

The invention also relates to the synthesis of synthetic polypeptides of the invention, in particular by chemical synthesis.

The polypeptides according to the present invention can be obtained by chemical synthesis using any of the numerous known peptide syntheses, for example the techniques using solid phases or techniques using partial solid phases, by condensation of fragments or by a conventional synthesis in solution.

Also forming part of the invention are the methods for the determination of the presence of a polynucleotide or a polypeptide encoded by involved in an protein-protein interaction of the present invention, characterized in that they use a polynucleotide or an antibody according to the invention.

These methods relate to, for example, the methods for the diagnosis *in vitro* of the presence in a biological sample of the procaryotic micro-organism from which said polypeptide is originating. The polynucleotide analysed may be either the genomic DNA, the cDNA or the mRNA.

These methods can use the probes and primers of the present invention.

The term "primer" denotes a specific oligonucleotide sequence which is complementary to a target nucleotide sequence and used to hybridize to the target nucleotide sequence. A primer serves as an initiation point for nucleotide polymerization catalyzed by either DNA polymerase, RNA polymerase or reverse transcriptase.

The term "probe" denotes a defined nucleic acid segment (or nucleotide analog segment, e.g., polynucleotide as defined hereinbelow) which can be used to identify a specific polynucleotide sequence present in samples, said nucleic acid segment comprising a nucleotide sequence complementary of the specific polynucleotide sequence to be identified.

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They are generally purified nucleic sequences for hybridization comprising at least 12 nucleotides, preferably at least 15, 20 and 25 nucleotides, characterized in that they can hybridize specifically with the polynucleotide chosen encoding the polypeptide of interest involved in an protein-protein interaction of the present invention.

Among the methods for the determination of the presence of a polynucleotide encoding a polypeptide of interest involved in an protein-protein interaction of the present invention, the methods comprising at least one stage for the so-called PCR (polymerase chain reaction) or PCR-like amplification of the target polynucleotide according to the invention with the aid of a pair of primers of nucleotide sequences according to the invention are preferred.

PCR-like will be understood to mean all methods using direct or indirect reproductions of nucleic acid sequences, or alternatively in which the labelling systems have been amplified, these techniques are of course known, in general they involve the amplification of DNA by a polymerase; when the original sample is an RNA, it is advisable to carry out a reverse transcription beforehand. There are currently a great number of methods allowing this amplification, for example the so-called NASBA "Nucleic Acid Sequence Based Amplification" (Compton J. 1991 Nature. 350 (6313): 91-92), TAS "Transcription based Amplification System" (Guatelli et al., 1990, Proc. Natl. Acad. Sci. USA. 35: 273-286), LCR "Ligase Chain Reaction" (Landegren et al., 1998, Genome Research, 8:769-776), "Endo Run Amplification" (ERA), "Cycling Probe Reaction" (CPR), and SDA "Strand Displacement Amplification" (Walker et al., Nucleic Acids Res. 20: 1691-1696, 1992), methods well known to persons skilled in the art.

The invention comprises, in addition, methods for the determination of the presence of a polypeptide of interest involved in an protein-protein interaction of the present invention, characterized in that an antibody according to the invention is brought into contact with the biological material to be tested, under conditions allowing the possible formation of specific immunological complexes between the said polypeptide and the said antibody, and in that the immuno-logical complexes possibly formed are detected, such as, for example, methods using RIA or ELISA.

The transformed cells as described above can also be used as models so as to study the interactions between a polypeptide of the invention and their interacting

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partners polypeptide, or between a polypeptide of the invention and chemical or protein compounds which are capable of modulating the protein-protein interaction according to the invention wherein said polypeptide of the invention is involved.

In particular, they may be used for the selection of products which interact with a polypeptide of the invention, or one of its SID® domains, as cofactor or as inhibitor, in particular a competitive inhibitor, or alternatively having an agonist or antagonist activity on the protein-protein interaction wherein said polypeptide of the invention is involved. Preferably, the said transformed cells will be used as a model allowing, in particular, the selection of products which make it possible to prevent and/or to treat pathologies induced by prokaryotic micro-organism.

Still another aspect of the invention pertains to a method for selecting an agent or compound capable of modulating the protein-protein interaction of a set of two polypeptides according to the invention comprising the steps of:

- a) cultivating a recombinant cell clone containing a reporter gene expression of which is toxic for said recombinant cell clone and transformed with two plasmids wherein:
 - i) the first plasmid contains a nucleic construct comprising a nucleic sequence encoding a first hybrid polypeptide containing one of said two polypeptides and a DNA binding domain;
 - ii) the second plasmid contains a nucleic construct comprising a nucleic sequence encoding a second hybrid polypeptide containing the second of said two polypeptides and an activating domain capable of activating said toxic reporter gene when the first and the second hybrid polypeptides are interacting;

on a selective medium containing the agent to be tested and allowing the growth of said recombinant cell clone when the toxic reporter gene is not activated; and

b) selecting agent which is capable of inhibiting the growth of the recombinant cell clone cultivated in step a).

The invention also comprises a method for selecting an agent or compound capable of modulating the protein-protein interaction of a set of two polypeptides according to the invention comprising the steps of:

a) cultivating a recombinant cell clone, preferably permeable, containing a reporter gene expression of which is toxic for said recombinant cell clone and transformed with two plasmids wherein:

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- i) the first plasmid contains a nucleic construct comprising a nucleic sequence encoding a first hybrid polypeptide containing one of said two polypeptides and the first domain of an enzyme;
- ii) the second plasmid contains a nucleic construct comprising a nucleic sequence encoding a second hybrid polypeptide containing the second of said two polypeptides and the second part of said enzyme capable of activating said toxic reporter gene when the first and the second hybrid polypeptides are interacting, said interaction restoring the activity of the enzyme;

on a selective medium containing the agent to be tested and allowing the growth of said recombinant cell clone when the toxic reporter gene is not activated; and

b) selecting agent which is capable of inhibiting the growth of the recombinant cell clone cultivated in step a).

In a preferred embodiment, said toxic reporter gene that can be used for negative selection, is URA3, CYH1 or CYH2 gene.

Still another aspect of the invention pertains to a method for selecting an agent or compound capable of modulating the protein-protein interaction of a set of two polypeptides according to the invention comprising the steps of:

- a) cultivating a recombinant cell clone containing a reporter gene expression of which stimulates the growth of said recombinant cell clone and transformed with two plasmids wherein:
 - i) the first plasmid contains a nucleic construct comprising a nucleic sequence encoding a first hybrid polypeptide containing one of said two polypeptides and a DNA binding domain;
 - ii) the second plasmid contains a nucleic construct comprising a nucleic sequence encoding a second hybrid polypeptide containing the second of said two polypeptides and an activating domain capable of activating said stimulating reporter gene when the first and the second hybrid polypeptides are interacting;

on a selective medium containing the agent to be tested and allowing the normal growth of said recombinant cell clone when the stimulating reporter gene is not activated; and

b) selecting agent which is capable of stimulating the growth of the recombinant cell clone cultivated in step a).

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In a preferred embodiment, the method according to the invention for selecting an agent or compound capable of modulating the protein-protein interaction of a set of two polypeptides is a method for selecting an agent capable of modulating the interaction between a polypeptide encoded by the ORF HP1198 (or a fragment thereof, preferably one of its SID® domains, or homologuous polypeptide thereof exhibiting at least 80 % identity degree) and a polypeptide encoded by the ORF HP1293 (or a fragment thereof, preferably one of its SID® domains, or homologuous polypeptide thereof exhibiting at least 80 % identity degree).

In a preferred embodiment, the method according to the invention for selecting an agent or compound capable of modulating the protein-protein interaction of a set of two polypeptides is a method for selecting an agent capable of modulating the interaction between a polypeptide encoded by the ORF HP1198 (or a fragment thereof, preferably one of its SID® domains, or homologuous polypeptide thereof exhibiting at least 80 % identity degree) and a polypeptide encoded by the ORF HP0088 (or a fragment thereof, preferably one of its SID® domains, or homologuous polypeptide thereof exhibiting at least 80 % identity degree).

In a preferred embodiment, the method according to the invention for selecting an agent or compound capable of modulating the protein-protein interaction of a set of two polypeptides is a method for selecting an agent capable of modulating the interaction between a polypeptide encoded by the ORF HP1198 (or a fragment thereof, preferably one of its SID® domains, or homologuous polypeptide thereof exhibiting at least 80 % identity degree) and a polypeptide encoded by the ORF HP1032 (or a fragment thereof, preferably one of its SID® domains, or homologuous polypeptide thereof exhibiting at least 80 % identity degree).

In another embodiment of the invention, inventors provide a kit for screening a modulator agent comprising at least one recombinant diploid clone or a cell clone, haploid or diploid, transformed with a plasmid containing a sequence coding for a bait polypeptide and a plasmid containing the nucleotide sequence of a SID® or of homologue polypeptide of SID®, said plasmids may be chosen between pACTIIst and pAS2ΔΔ.

SID® or homologue sequence of SID® acting on the same pair of interacting proteins may be also modulator agents.

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Modulator agent selected by anyone of the yeast or bacterial two-hybrid system method of the invention also forms part of the invention.

These modulator agents of protein-protein interaction according to the invention may be obtained for example from a library of compounds.

Consequently, is also part of the invention a modulator agent selected by the method of the invention previously described capable of interfering with a protein-protein interaction according to the invention. This agent may modulate an interaction of the invention between two prokaryotic polypeptides, particularly between two Helicobacter pylori, Escherichia coli, Staphylococcus aureus or Streptococcus pneumoniae polypeptides, or between a prokaryotic polypeptide, such as Helicobacter pylori, Staphylococcus aureus or Streptococcus pneumoniae polypeptide, and a polypeptide originating from a host organism of said prokaryotic micro-organism, such as mammal, particularly human.

These methods allow the selection of chemical or biochemical compound capable of interacting, directly or indirectly, with the polynucleotide or the polypeptide encoded by of the invention, in particular capable of modulating the protein-protein interaction wherein said polypeptide of the invention is involved.

More particularly, the invention concerns modulator agent capable of modulating, more preferred of inhibiting, the viability and/or the growth of the prokaryotic micro-organism, preferrably *Helicobacter pylori*, *Staphylococcus aureus* or *Streptococcus pneumoniae*, from which is the protein-protein interaction.

For the screening of compounds capable of modulating the protein-protein interaction wherein said polypeptide of the invention is involved, the preferred principal effect is the effect of inhibiting the viability and/or the growth of the prokaryotic microorganism, preferrably *Helicobacter pylori*, *Staphylococcus aureus* or *Streptococcus pneumoniae*, from which is the protein-protein interaction.

These effects of modulating the viability and/or the growth of prokaryotic microorganisms can be analysed by any method known by a skilled man.

For example, a screening method of modulating agent can comprise the following steps:

- Select one specific interaction.

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- Transform a permeabilized yeast cell with plasmids containing bait polypeptide and prey polypeptide of the specific interaction.
- Plate a top agar containing transformed permeabilized yeast cells on square boxes (that already contains agarose gel).
 - Apply by spotting the compounds to test on top agar as soon as it is solidified.
 - Incubate, for example overnight at 30°C, and
- Analyse results : select lead compounds that prevent transformed permeabilized yeast cells from growing.

Screening may be used to test compounds capable of modifying the level and/or the specificity of expression of the polynucleotide or the polypeptide encoded by of the invention involved in the protein-protein interaction according to the invention.

A quantitative or qualitative analysis of the expression of the gene encoded the polypeptide of the invention involved in the protein-protein interaction according to the invention can be carried out using primers or probes of the invention as DNA templates, the term DNA templates designating nucleic acids having a sufficient length to allow a specific detection of the expression of mRNAs capable of hybridizing thereto. For example, the DNA templates contain nucleic acids derived from said gene, or sequences complementary thereto for which it is desired to estimate the level or the specificity of expression, and comprising at least 15, at least 25, at least 50, at least 100 or at least 500 consecutive nucleotides.

Another aspect of the present invention consists in methods of identifying molecules capable of binding to one of the set of two polypeptides of the invention involved in the protein-protein interaction. Such molecules can be used to modulate the viability and/or the growth of the prokaryotic micro-organism, preferrably *Helicobacter pylori*, from which is the protein-protein interaction activity. For example, such molecules can be used to stimulate or to inhibit a biological reaction involved in the viability and/or the growth of the prokaryotic micro-organism.

Numerous methods well known by the skilled man exist for identifying ligands for a defined polypeptide.

For example to identifying molecules capable of binding to one polypeptide of the set of two polypeptides of the invention involved in the protein-protein interaction, a subunit thereof or a fragment thereof comprising at least 10, at least 20, at least 30, or

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more than 30 consecutive amino acids with small molecules such as those generated by combinatory chemistry, it is possible to use an HPLC-coupled microdialysis, or an affinity capillary electrophoresis.

In other methods, the peptides or small molecules capable of interacting with said one of the set of two polypeptides of the invention, a subunit thereof or a fragment thereof may be linked to detectable markers such as radioactive, fluorescent or enzymatic markers. These labelled molecules are brought into contact with the immobilized said one of the set of two polypeptides of the invention, under conditions allowing a specific interaction. After elimination of the molecules which are not specifically bound, the bound molecules are detected by appropriate means.

In addition, the peptides or small molecules which bind to said one of the set of two polypeptides of the invention, preferably to its SID® binding site can be identified by competition experiments. In such experiments, said one of the set of two polypeptides of the invention, is immobilized on a surface. Increasing quantities of peptides or of small molecules are brought into contact with the immobilized said one of the set of two polypeptides of the invention in the presence of the second labelled polypeptide of said two polypeptides of the invention, designated labelled ligand. The labelled ligand may be labelled with a radioactive, fluorescent or enzymatic marker. The capacity of the molecule tested to interact with said one of the set of two polypeptides of the invention is determined by measuring the quantity of labelled ligand bound in the presence of the molecule tested. A decrease in the quantity of bound ligand when the molecule tested is present indicates that the latter is capable of interacting with said one of the set of two polypeptides of the invention.

The Biacore™ technology can also be used to carry out the screening of compounds capable of interacting with said one of the set of two polypeptides of the invention. This technology is described in Szabo et al. (1995) and in Edwards and Leartherbarrow (Analytical Biochemistry, 246, 1-6, 1997), of which the teaching is incorporated by reference, and makes it possible to detect interactions between molecules in real time without the use of labelling.

One of the main advantages of this method is that it allows the determination of the association constants between said one of the set of two polypeptides of the

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invention and the interacting molecules. Thus, it is possible to specifically select the molecules interacting with high or low association constants.

The proteins or other molecules interacting said one of the set of two polypeptides of the invention can be identified using affinity columns which contain said one of the set of two polypeptides of the invention. Said one of the set of two polypeptides of the invention may be attached to the column using conventional techniques including chemical coupling to an appropriate column matrix such as agarose, Affi Gel, or other matrices known to a person skilled in the art. In another aspect of the invention, the affinity column may contain chimeric proteins in which said one of the set of two polypeptides of the invention would be fused, for example, with glutathione S-transferase. The molecules to be tested which are described above are then deposited on the column. The molecules interacting said one of the set of two polypeptides of the invention are retained by the column and can be isolated by elution.

The chemical or biochemical compounds, characterized in that they make it possible to modulate, directly or indirectly, the protein-protein interaction according to the invention, and selected by the said methods defined above, also form part of the invention.

The use of a polypeptide according to the invention for the modulation of *Helicobacter pylori*'s protein interaction, also forms part of the present invention.

Still another aspect, the present invention is directed to a method for the production of monoclonal or polyclonal antibodies comprising the step of immunization of an animal or human organism with an immunogenic agent comprising a polypeptide, a vector according or a host cell according to the invention, and to antibodies obtained by said method.

The mono- or polyclonal antibodies or fragments thereof, chimeric or immunoconjugated antibodies, characterized in that they are capable of specifically recognizing a polypeptide according to the invention, also form part of the invention.

As used herein, the term "antibody" refers to a polypeptide or group of polypeptides which are comprised of at least one binding domain, where an antibody binding domain is formed from the folding of variable domains of an antibody molecule to form three-dimensional binding spaces with an internal surface shape and charge distribution complementary to the features of an antigenic determinant of an antigen,

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which allows an immunological reaction with the antigen. Antibodies include recombinant proteins comprising the binding domains, as wells as fragments, including Fab, Fab', F(ab)2, and F(ab')2 fragments.

Specific polyclonal antibodies may be obtained from a serum of an animal immunized against a polypeptide according to the invention, in particular produced by genetic recombination or by peptide synthesis, according to the customary procedures, from a polynucleotide according to the invention.

The specific monoclonal antibodies may be obtained according to the conventional hybridoma culture method described by Kohler and Milstein (Kohler, G. and Milstein, C., Nature 256:495, 1975).

The antibodies according to the invention are, for example, chimeric antibodies, humanized antibodies, Fab or F(ab')2 fragments. They may also be in the form of immunoconjugates or of labelled antibodies so as to obtain a detectable and/or quantifiable signal (Harlow, E., and D. Lane. 1988. Antibodies A Laboratory Manual. Cold Spring Harbor Laboratory. pp. 53-242).

The invention also relates to methods for the detection and/or purification of a polypeptide according to the invention, characterized in that they use an antibody according to the invention.

The invention comprises, in addition, purified polypeptides, characterized in that they are obtained by a method according to the invention.

Moreover, in addition to their use for the purification of polypeptides, the antibodies of the invention, in particular the monoclonal antibodies, may also be used for the detection of these polypeptides in a biological sample.

They thus constitute a means for the immunocytochemical or immunohistochemical analysis of the expression of polypeptide against which they are raised on specific tissue sections, for example by immunofluorescence, gold labelling, enzymatic immunoconjugates.

They make it possible in particular to detect expression of these polypeptides in the biological tissues or samples, which makes them useful for monitoring the progress of a method of prevention or treatment.

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More generally, the antibodies of the invention may be advantageously used in any situation where the expression of a polypeptide of the invention against which they are raised needs to be observed.

The invention finally relates to a polynucleotide, a polypeptide, a vector, a host cell, a modulator agent or an antibody to the invention as compound for the preparation of a medicament.

So the invention also encompasses a pharmaceutical composition comprising a compound selected from the group consisting of:

- a) a polynucleotide according to the invention;
- 10 b) a polypeptide according to the invention;
 - c) a vector according to the invention;
 - d) a host cell according to the invention;
 - e) a modulator agent to the invention; and
 - f) an antibody to the invention.

A pharmaceutical composition according to the invention, wherein said composition is administered by any route such as intravenous route, intramuscular route, oral route, or mucosal route with an acceptable physiological carrier and/or adjuvant, also forms part of the invention.

The compounds according to the invention as a medicament for the prevention and/or treatment of pathologies of infection diseases induced by prokaryotic microorganism are particularly preferred.

The most preferred are the compounds according to the invention, as a medicament for the prevention and/or treatment of infection diseases induced by Helicobacter pylori, Staphylococcus aureus or Streptococcus pneumoniae.

The compounds of the invention as active ingredients of a medicament will be preferably in soluble form, combined with a pharmaceutically acceptable vehicle.

Such compounds which can be used as a medicament offer a new approach for preventing and/or treating pathologies linked to infection by prokaryotic microorganism such as *Helicobacter pylori*, *Staphylococcus aureus* or *Streptococcus pneumoniae*. Preferably, these compounds will be administered by the systemic route, in particular by the intravenous route, by the intramuscular or intradermal route or by the oral route.

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Their modes of administration, optimum dosages and galenic forms can be determined according to the criteria generally taken into account in establishing a treatment suited to a patient, such as for example the age or body weight of the patient, the seriousness of his general condition, the tolerance to treatment and the side effects observed, and the like.

The identified compounds can be administered to a mammal, including a human patient, alone or in pharmaceutical compositions where they are mixed with suitable carriers or excipient(s) at therapeutically effective doses to treat disorders associated with prokaryotic micro-organism infection. Techniques for formulation and administration of the compounds of the instant application may be found in "Remington's Pharmaceutical Sciences", Mack Publishing Co., Easton, PA, latest edition.

Suitable routes of administration include oral, rectal, transmucosal, or intestinal administration, parenteral delivery, including intramuscular, subcutaneous, injections, as well as intravenous, intraperitoneal or intranasal injections.

Pharmaceutical compositions and medicaments for use in accordance with the present invention may be formulated in a conventional manner using one or more physiologically acceptable carriers comprising excipients and auxiliaries. Proper formulation is dependent upon the route of administration chosen.

For injection, the agents of the invention may be formulated in aqueous solutions, preferably in physiologically compatible buffers such as Hanks's solution, Ringer's solution, or physiological saline buffer such as a phosphate or bicarbonate buffer. For transmucosal administration, penetrants appropriate to the barrier to be permeated are used in the formulation. Such penetrants are generally known in the art.

Pharmaceutical preparations which can be used orally include push-fit capsules made of gelatin, as well as soft, sealed capsules made of gelatin and a plasticizer, such as glycerol or sorbitol. The push-fit capsules can contain the active ingredients in admixture with fillers such as lactose, binders such as starches, and/or lubricants such as talc or magnesium stearate and, optionally, stabilizers. In soft capsules, the active compounds may be dissolved or suspended in suitable liquids, such as fatty oils, liquid paraffin, or liquid polyethylene glycols. In addition, stabilizers may be added. All

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formulations for oral administration should be in dosages suitable for such administration.

For buccal administration, the compositions may take the form of tablets or lozenges formulated in conventional manner.

For administration by inhalation, the compounds for use according to the present invention are conveniently delivered in the form of an aerosol spray presentation from pressurized packs or a nebulizer, with the use of a suitable gaseous propellant, e.g., carbon dioxide. In the case of a pressurized aerosol the dosage unit may be determined by providing a valve to deliver a metered amount. Capsules and cartridges of, e.g., gelatin, for use in an inhaler or insufflator, may be formulated containing a powder mix of the compound and a suitable powder base such as lactose or starch.

The compounds may be formulated for parenteral administration by injection, e.g., by bolus injection or continuous infusion. Formulations for injection may be presented in unit dosage form, e.g., in ampoules or in multi-dose containers, with an added preservative. The compositions may take such forms as suspensions, solutions or emulsions in aqueous vehicles, and may contain formulatory agents such as suspending, stabilizing and/or dispersing agents.

Pharmaceutical formulations for parenteral administration include aqueous solutions of the active compounds in water-soluble form. Aqueous suspensions may contain substances which increase the viscosity of the suspension, such as sodium carboxymethyl cellulose, sorbitol, or dextran. Optionally, the suspension may also contain suitable stabilizers or agents which increase the solubility of the compounds to allow for the preparation of highly concentrated solutions.

Alternatively, the active ingredient may be in powder or lyophilized form for constitution with a suitable vehicle, such as sterile pyrogen-free water, before use.

Additionally, the compounds may be delivered using a sustained-release system, such as semipermeable matrices of solid hydrophobic polymers containing the therapeutic agent. Various sustained-release materials have been established and are well known by those skilled in the art. Sustained-release capsules may, depending on their chemical nature, release the compounds for a few weeks up to over 100 days.

Depending on the chemical nature and the biological stability of the therapeutic reagent, additional strategies for protein stabilization may be employed.

The pharmaceutical compositions also may comprise suitable solid or gel phase carriers or excipients. Examples of such carriers or excipients include but are not limited to calcium carbonate, calcium phosphate, various sugars, starches, cellulose derivatives, gelatin, and polymers such as polyethylene glycols.

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Pharmaceutical compositions suitable for use in the present invention include compositions wherein the active ingredients are contained in an effective amount to achieve their intended purpose. More specifically, a therapeutically effective amount means an amount effective to prevent development of or to alleviate the existing symptoms of the subject being treated. Determination of the effective amounts is well within the capability of those skilled in the art, especially in light of the detailed disclosure provided herein.

For any compound used in the method of the invention, the therapeutically effective dose can be estimated initially from cell culture assays. For example, a dose can be formulated in animal models to achieve a circulating concentration range that includes or encompasses a concentration point or range shown the desired effect in an in vitro system. Such information can be used to more accurately determine useful doses in humans.

A therapeutically effective dose refers to that amount of the compound that results in amelioration of symptoms in a patient. Toxicity and therapeutic efficacy of such compounds can be determined by standard pharmaceutical procedures in cell cultures or experimental animals, e.g., for determining the LD50, (the dose lethal to 50 % of the test population) and the ED50 (the dose therapeutically effective in 50 % of the population). The dose ratio between toxic and therapeutic effects is the therapeutic index and it can be expressed as the ratio between LD50 and ED50. Compounds which exhibit high therapeutic indices are preferred.

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The data obtained from these cell culture assays and animal studies can be used in formulating a range of dosage for use in human. The dosage of such compounds lies preferably within a range of circulating concentrations that include the ED50, with little or no toxicity. The dosage may vary within this range depending upon the dosage form employed and the route of administration utilized. The exact formulation, route of administration and dosage can be chosen by the individual physician in view of the

patient's condition (see, e.g., Fingl et al., 1975, in "The Pharmacological Basis of Therapeutics", Ch. 1).

Dosage amount and interval may be adjusted individually to provide plasma levels of the active compound which are sufficient to maintain the modulating effects. Dosages necessary to achieve the modulating effect will depend on individual characteristics and route of administration.

The amount of composition administered will, of course, be dependent on the subject being treated, on the subject's weight, the severity of the affliction, the manner of administration and the judgment of the prescribing physician.

Other characteristics and advantages of the invention appear in the remainder of the description with the examples and figures whose legends are represented below.

Examples

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Medium composition and standard protocols are available in Sambrook and Maniatis (Sambrook, J., Fritsch, E.F., and T. Maniatis. (1989) Molecular Cloning: A Laboratory Manual. 2ed. Cold Spring Harbor Laboratory, Cold Spring Harbor, New York).

Example 1: Preparation of a Helicobacter pylori genomic collection

1.A. Collection preparation and transformation in Escherichia coli

1, A.1. Fragmented of genomic DNA preparation

The *Helicobacter pylori* genomic DNA is fragmented in a nebulizer (GATC) for 1 minute, precipitated and resuspended in water.

The obtained nebulized genomic DNA is successively treated with Mung Bean Nuclease (Biolabs) (30 minutes at 30°C), T4 DNA polymerase (Biolabs) (10 minutes at 37°C) and Klenow enzyme (Pharmacia) (10 minutes at room temperature and 1 hour at 16°C).

DNA is then extracted, precipitated and resuspended in water.

1.A.2. Ligation of linkers to blunt-ended genomic DNA

Oligonucleotide PL160 (5' end phosphorylated) 1 μ g/ μ l and PL159 2μ g/ μ l.

Sequence of the oligo PL160: 5'-ATCCCGGACGAAGGCC-3'.

Sequence of the oligo PL159: 5'-GGCCTTCGTCCGG-3'.

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Linkers were preincubated (5 minutes at 95°C, 10 minutes at 68°C, 15 minutes at 42°C) then cooled down at room temperature and ligated with genomic DNA inserts at 4°C overnight.

Linkers were further removed on a separation column (Chromaspin TE 400, Clontech), according to the manufacturer protocol.

1.A.3. Vector preparation

pACTIIst is successively digest with BamHI restriction enzyme (Biolabs) for 1 hour at 37°C, dephosphorylated with Calf Intestine Phosphatase (CIP) (Biolabs) and filled in with dGTP using Vent DNA polymerase (exo-) (Biolabs), extracted, precipitated and resuspended in water.

1.A.4. Ligation between vector and insert of genomic DNA

The prepared vector is ligated overnight at 15°C with the genomic blunt ended DNA described in section 2 using T4 DNA ligase (Biolabs). The DNA is then precipitated and resuspended in water.

1.A.5. Library transformation in Escherichia coli

Transform DNA from section 1.A.4 into Electromax DH10B electrocompetent cells (Gibco BRL) with Cell Porator apparatus (Gibco BRL). Add 1 ml SOC medium and incubate transformed cells at 37°C for 1 hour. Add 9 ml volume of SOC medium per tube and plate on LB+ampicillin medium. Scrape colonies with liquid LB medium. Aliquot and freeze at -80°C.

The obtained collection of recombinant cell clones is named HGXBHP1 (CNCM No I-2181 deposited on April 13, 1999).

1.B. Collection transformation in Saccharomyces cerevisiae

The Saccharamyces cerevisiae strain (Y187 (MATα Gal4Δ Gal80Δ ade2-101 His3 Leu2-3, -112 Trp1-901 Ura3-52 URA3::UASGAL1-LacZ Met)) transformed with the HGXBHP1 H. pylori genomic DNA library.

The plasmid DNA contained in *E. coli* are extracted (Qiagen) from aliquoted *E. coli* frozen cells (1.A.5.).

Grow Saccharomyces cerevisiae yeast Y187 in YPGlu.

Yeast transformation is performed according to standard protocol (Giest et al. Yeast, 11, 355-360, 1995) using yeast carrier DNA (Clontech). This experiment leads to

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10⁴ to 5.10⁴ cells/μg DNA. Spread an estimating of 2.10⁴ transformanton DO-Leu (Drop-out) medium per plates. Aliquot and freeze at -80°C.

1.C. Construction of bait plasmid

The genomic amplification of the ORF is obtained by PCR using the Pfu proofreading Taq polymerase (Stratagene) and 200 ng of genomic DNA as template. PCR primers are chosen in regions flanking the ORF.

Set up the PCR program as followed:

Check amplification on agarose gel.

Purify PCR fragments with Qiaquick column (Qiagen) according to the manufacturer protocol.

Digest purified PCR fragments with adequate restriction enzymes.

Purify PCR fragments with Qiaquick column (Qiagen) according to the manufacturer protocol.

Ligate digested PCR fragments into an adequately digested and dephosphorylated bait vector (pAS2 $\Delta\Delta$) according to standard protocol (Maniatis et al.).

Transform into competent bacterial cells. Grow cells, extract DNA and sequence plasmid.

This protocole may also be applied to E. coli, S. aureus and S. pneumoniae genomic DNA.

Example 2: Screening the collection with the two-hybrid in yeast system

2.A. The mating protocol

We have chosen the mating two-hybrid in yeast system (firstly described by Fromont Racine et al., Nature Genetics, 1997, vol. 16, 277-282, Toward a functional analysis of the yeast genome through exhaustive two-hybrid screens) for its advantages but we could also screen the *Helicobacter pylori* collection in classical two-hybrid system as described in Fields *et al.* or in a yeast reverse two-hybrid system.

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The mating procedure allows a direct selection on selective plates because the two fusion proteins are already produced in the parental cells. No replica plating is required.

This protocol is written for the use of the library transformed into the Y187 strain.

Before mating, transform S. cerevisiae (CG 1945 strain (MATa Gal4-542 Gal180-538 ade2-101 His3*200 Leu2-3,-112 Trp1-901 Ura3-52 Lys2-801 URA3::GAL4 17mers (X3)-CyC1TATA-LacZ LYS2::GAL1UAS-GAL1TATA-HIS3 CYH^R)) according to step 1.B. and spread on DO-Trp medium.

10 Day 1, morning: preculture

Preculture of Y187 cells carrying the bait plasmid obtained at step 1.C. in 20 ml DO-Trp medium. Grow at 30°C with vigorous agitation.

Day 1, late afternoon: culture

Measure OD_{600nm} of the DO-Trp preculture of Y187 cells carrying the bait plasmid preculture.

Inoculate 150 ml DO-Trp at OD600nm 0.006/ml, grow overnight at 30°C with vigorous agitation.

Day 2: mating

medium and plates

20 5 YPGlu plates (Rich medium with glucose)

50 ml tube with 30 ml DO-Leu-Trp-His

100 ml flask with 20 ml of YPGlu

75 DO-Leu-Trp-His plates

2 DO-Leu plates

25 2 DO-Trp plates

2 DO-Leu-Trp plates

Measure OD_{600nm} of the DO-Trp culture. It should be around 1.

For the mating, you must use twice as many bait cells as library cells. To get a good mating efficiency, you must collect the cells at 10⁸ cells per cm².

Estimate the amount of bait culture (in ml) that makes up 80 OD600nm units for the mating with the prokaryote library.

Thaw a vial containing the HGXYHP1 library slowly on ice. Add the contents of the vial to 20 ml YPGlu. Let those cells recover at 30°C, under gentle agitation for 10 minutes.

Mating

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Put the 80 OD600nm units of bait culture into a 250 ml flask.

Add the HGXYHP1 library culture to the bait culture. Transfer the mixture of diploids into 50 ml sterile tubes. Centrifuge, discard the supernatant and resuspend in YPGlu medium.

Distribute cells on YPGlu Plates (Rich medium with glucose).

Incubate plates cells-up at 30°C for 4h30min.

Collection of mated cells

Wash and rinse plates and spread collected cells on DO-Leu-Trp-His plates.

Day 4

Selection of clones capable of growing on DO-Leu-Trp-His: this medium allows us to isolate diploid clones presenting an interaction.

Count the His+ colonies on control plates.

The number of His+ cell clones will define which protocol is to be processed : Upon 20.10^6 His+ colonies :

- if number of His+ cell clones > 285: then process overlay and then luminometry protocols on blue colonies (2.B and 2.C);
- if number of His+ cell clones < 285: process luminometry protocol (2.C).

The following step leads to the selection of the strongest interaction.

2.B. The X-Gal overlay assay

X-Gal overlay assay is performed directly on the selective medium plates after scoring the number of His⁺ colonies.

Material

Set up a waterbath. The water temperature should be 50°C.

- 0.5 M Na₂HPO₄ pH 7.5.
- 1,2 % Bacto-agar.
- 30 2 % X-Gal in DMF (dimethyl formamide).

- Overlay mixture: 0.25 M Na₂HPO₄ pH7.5, 0.5 % agar, 0.1 % SDS (Sodium dodecyl sulfate), 7 % DMF (LABOSI), 0.04 % X-Gal (ICN). For each plate, 10 ml overlay mixture are needed.
- DO-leu-trp-his plates.
- Sterile toothpicks.

Experiment

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Temperature of the overlay mix should be between 45 and 50°C.

Pour the overlay-mix over the plates in portions of 10 ml.

Collect them when the top layer is settled.

Incubate plates overlay-up at 30°C. Note the time.

Check for blue colonies regularly. If no blue colony appears, wait for overnight incubation. Mark with a pen and number the positives.

Streak the positives colonies on fresh DO-Leu-Trp-His plates with a sterile toothpick.

15 2.C. The luminometry assay

Grow His+ colonies overnight at 30°C in microtiter plates containing DO-Leu-Trp-His+Tetracyclin medium with shaking. The day after, dilute 15 times overnight culture into a new microtiter plate containing the same medium. Incubate 5 hours at 30°C with shaking. Dilute samples 5 times and read OD_{600nm}. Dilute again to obtain between 10 000 and 75 000 yeast cells/well in 100 μl final volume.

Per well, add 76 μl of One Step Yeast Lysis Buffer (Tropix), 20 μl SapphireII Enhancer (Tropix), 4 μl Galacton Star (Tropix), incubate 40 minutes at 30°C.

Measure the β -Gal read-out (L) using a Luminometer (Trilux, Wallach).

Calculate value of OD_{600nm}/L and select interacting preys having highest values.

At this step of the protocol, we have isolated diploid cell clones presenting interaction. The next step is now to identify polypeptides involved in the selected interactions.

Example 3: Identification of positive clones

3.A. PCR on yeast colonies

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Introduction

PCR amplification of fragments of plasmid DNA directly on yeast colonies is a quick and efficient procedure to identify sequences cloned into this plasmid. It is directly derived from a published protocol (Wang H. et al., Analytical Biochemestry, 237, 145-146, 1996). However, it is not a standardized protocol: in our hands it varies from strain to strain, it is dependent of experimental conditions (number of cells, Taq polymerase source, etc). This protocol should be optimized to specific local conditions. Materials

- For 1 well, PCR mix composition is:

 $32.5 \mu l$ water,

5 μl 10X PCR buffer (Pharmacia),

1 µl dNTP (10 mM each)

- 0.5 µl Taq polymerase (5u/µl) (Pharmacia),
- 0.5 µl oligonucleotide ABS1 10 pmole/µl: 5'-GCGTTTGGAATCACTACAGG-3',
- 0.5 μl oligonucleotide ABS2 10 pmole/μl: 5'-CACGATGCACGTTGAAGTG-3'.

- 1 N NaOH.

Experiment

Grow positive colonies overnight at 30°C on a 96 well cell culture cluster (Costar), containing 150 μ l DO-Leu-Trp-His+Tetracyclin with shaking. Resuspend culture and transfer immediately 100 μ l on a Thermowell 96 (Costar).

Centrifuge 5 minutes at 4000 rpm at room temperature.

Remove supernatant.

Place the Thermowell in the thermocycler (GeneAmp 9700, Perkin Elmer) 5 minutes at 99.9°C and then 10 minutes at 4°C.

Add lysis buffer and incubate.

Centrifuge, transfer aliquot of supernatant in each well, add PCR mix, shake well.

Set up the PCR program as followed:

	94°C	3 minutes	
30	94°C	30 secondes	
	53°C	1 minute 30 secondes	x 35 cycles
	72°C	3 minutes	

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72°C 5 minutes

15°C °

Check the quality, the quantity and the length of the PCR fragment on agarose gel.

The length of the cloned fragment is the estimated length of the PCR fragment minus 300 base pairs that correspond to the amplified flanking plasmid sequences.

3.B. Plasmids rescue from yeast by electroporation

Introduction

The previous protocol of PCR on yeast cell may not be successful, in such a case, we rescue plasmids from yeast by electroporation. This experiment allows the recovery of prey plasmids from yeast cells by transformation of *E. coli* with a yeast cellular extract. We can then amplify the prey plasmid and sequence the cloned fragment.

Material

15 Plasmid rescue

Glass beads 425-600 µm (Sigma)

Phenol/chloroform (1/1) premixed with isoamyl alcohol (Amresco)

Extraction buffer: 2 % Triton X100, 1 % SDS, 100 mM NaCl, 10 mM TrisHCl pH 8.0, 1 mM EDTA pH 8.0.

Mix ethanol/NH₄Ac: 6 volumes ethanol with 7.5 M NH₄ Acetate, 70 % Ethanol and yeast cells in patches on plates.

Electroporation

SOC medium

M9 medium

Selective plates: M9-Leu+Ampicillin

2 mm electroporation cuvettes (Eurogentech)

Experiment

Plasmid rescue

Prepare cell patch on DO-Leu-Trp-His with cell culture of section 2.C.

Scrape the cell of each patch in Eppendorf tube, add 300 µl of glass beads in each tube, then, add 200 µl extraction buffer and add 200 µl phenol:chloroform:isoamyl alcohol (25:24:1).

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Centrifuge tubes 10 minutes at 15000 rpm.

Transfer 180 µl supernatant to a sterile Eppendorf tube and add to each 500 µl ethanol/NH₄Ac, vortex.

Centrifuge tubes 15 minutes, 15000 rpm at 4°C.

Wash pellet with 200 μ l 70 % ethanol, remove ethanol and dry pellet.

Resuspend pellet in 10 µl water. Store extracts at -20°C.

Electroporation

Material: Electrocompetent MC1066 cells prepared according to standard protocols (Maniatis).

10 Add 1 µl of yeast plasmid DNA-extract to pre-chilled Eppendorf tube, and keep on ice.

Mix 1 μ l plasmid yeast DNA-extract sample, add 20 μ l electrocompetent cells and transfer in a cold electroporation cuvette.

Set the Biorad electroporator on 200 ohms resistance, 25 μF capacity; 2.5 kVolts.

Place cuvette in the cuvette holder and electroporate.

Add 1 ml SOC into the cuvette and transfer the cell-mix into sterile Eppendorf tube.

Let cells recover for 30 minutes at 37°C, spin the cells down 1 minute, 4000x g and pour off supernatant. Keep about 100 µl medium and use it to resuspend the cells and spread them on selective plates (e.g. M9-Leu plates).

Incubate plates for 36 hours at 37°C.

Grow one colony and extract plasmids. Check presence and size of insert through enzymatic digestion and agarose gel. Sequence insert.

Example 4: Protein-Protein Interactions

For the purpose of this example, we have chosen to study *Helicobacter pylori*'s protein-protein interactions.

For each bait, the previous protocol leads to the identification of prey polynucleotide sequences. In order to identify a protein-protein interaction, we need to characterize the obtained prey polypeptide sequence regarding the *Helicobacter pylori* genome.

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This may be accomplish with a software program names blastwun (available on the Internet site of the University of Washington : http://bioweb.pasteur.fr/seqanal/interfaces/blastwu.html, this is a development version of software for gene and protein identification through similarity searches of protein and nucleotide sequence databases).

Blastwun program compares prey polypeptide insert sequence (rescued from prey plasmid) with whole *Helicobacter pylori* genome (available on N.C.B.I. web site: http://www.ncbi.nlm.nih.gov under GenBank accession number AE000511). This comparison leads to prey polynucleotide localizations in *H. pylori* genome, each localization having a score depending on the homology of sequence. For each prey polynucleotide, we consider the localization with the highest score and, if the insert sequence is included in and is in phase with an Open Reading Frame, we can identify one prey polypeptide interacting with one bait polypeptide.

Helicobacter pylori ORF's sequences are available on the World-Wide Web site of The Institute for Genomic Research (TIGR) at http://www.tigr.org/tdb/mbd/hpdb/hpdb.html.

This web page allows several request concerning Helicobacter pylori's genome, in particular, its ORF sequence. To get the sequences of a specific ORF, click on the window named «HP#» and click search. This operation leads to a new web page presenting nucleic and peptide sequence of the specific ORF.

Table I: protein interaction in Helicobacter pylori (see hereafter)

Example 5: Identification of SID®

Experiment results in step 4. sequences of each prey fragment encoding for an interacting prey polypeptide.

By comparing and selecting the intersection of every isolated fragments that are included in the same polypeptide, we define the Selected Interacting Domain (SID®) see figure 7.

30 See results in Tables II and III.

<u>Table I</u>: Interaction involving polypeptides including *Helicobacter pylori* ORF

Bait polypeptides	Interacting ORF
(ORF reference according to Tomb et al.)	(ORF reference according to Tomb et al.)
HP0047	HP0047
HP0047	HP0048
HP0047	HP0695
HP0061	HP0066
HP0061	HP0978
HP0061	HP1409
HP0064	HP0063
HP0066	HP0066
HP0067	HP0069
HP0067	HP0609
HP0067	HP0768
HP0067	HP0770
HP0067	HP0956
HP0068	HP0070
HP0068	HP0118
HP0069	HP0067
HP0070	HP0068
HP0070	HP0070
HP0071	HP0278
HP0071	HP0417
HP0071	HP0570
HP0071	HP0775
HP0071	HP1340
HP0071	HP1409
HP0072	HP1489
HP0073	HP0073
HP0073	HP0232

HP0073	HP0259
HP0073	HP0067
HP0073	HP0232
HP0073	HP0705
	HP1198
HP0268	HP0289
HP0289	
HP0289	HP0289
HP0289	HP0887
HP0289	HP0922
HP0289	HP1038
HP0289	HP1543
HP0289	HP0289
HP0289	HP0289
HP0289	HP0610
HP0289	HP1355
HP0311	HP0312
HP0338	HP0132
HP0338	HP0337
HP0391	HP0099
HP0391	HP0392
HP0691	HP0692
HP0691	HP1362
HP0697	HP0012
HP0697	HP0048
HP0697	HP0558
HP0697	HP0599
HP0697	HP0696
HP0697	HP0864
HP0697	HP1037
	HP1038
HP0697	HP1299
HP0697	IV 1277

HP0697	HP1576
HP0776	HP0067
HP0776	HP0278
HP0776	HP1378
HP0776	HP1409
HP0797	HP0289
HP0797	HP0887
HP0797	HP1349
	HP1377
HP0797	HP1409
HP0797	HP0433
HP0800	HP0687
HP0800	
HP0800	HP0800
HP0800	HP0801
HP0800	HP0924
HP0800	HP1267
HP0800	HP1460
HP0801	HP0152
HP0801	HP0800
HP0801	HP1513
HP0868	HP0088
HP0868	HP0327
HP0868	HP0869
HP0868	HP1142
HP0874	HP0875
HP0875	HP0874
HP0887	HP0459
HP0887	HP0610
HP0887	HP0699
HP0887	HP0887
HP0887	HP1157
111 0007	

HP0887	HP1460
HP0887	HP1464
HP0887	HP0610
HP0887	HP0887
HP0887	HP1157
HP0887	HP1464
HP0935	HP0072
HP0935	HP0528
HP0935	HP0657
HP0978	HP0979
HP0978	HP1583
HP1032	HP0643
HP1032	HP0818
HP1032	HP1122
HP1032	HP1198
HP1032	HP1316
HP1067	HP0392
HP1198	HP0088
HP1198	HP0268
HP1198	HP0293
HP1198	HP0452
HP1198	HP0705
HP1198	HP0775
HP1198	HP0965
HP1198	HP1032
HP1198	HP1114
HP1198	HP1124
HP1198	HP1198
HP1198 .	HP1274
HP1198	HP1378
HP1198	HP1411

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HP1198	HP1541
HP1198	HP1032
HP1198	HP1218
HP1230	HP1230
HP1230	HP1529
HP1231	HP1247
HP1244	HP0857
HP1244	HP1246
HP1246	HP0121
HP1246	HP0326
HP1246	HP0407
	HP0886
HP1246	
HP1246	HP1035
HP1246	HP1244
HP1246	HP1460
HP1247	HP1231
HP1247	HP1353
HP1293	HP1198

^{*} Tomb et al., 1997, Nature, 388, 539-547

As indicated page 547 in the document Tomb et al., the annotated *H. pylori* genome sequence and gene family alignments are avalaible on the World-Wide Web site at http://www.tigr.org/tdb/mbd/hpdb/hpdb/hpdb.html. For each ORF referenced HPXXXX, the detailed nucleic sequence, and amino acids sequence encoded by, can be obtained on the World-Wide Web site at http://www.tigr.org/tdb/mbd/hpdb/hpdb.html. by introducing said reference HPXXXX (see example 4).

Table II:

Bait polypeptides	SID®
(ORF reference according to Tomb et al.)	Amino Acid Sequence (SEQ ID N°)
HP0868	2
HP0868	4
HP0868	6
HP0868	8
HP0800	10
HP0800	12
HP0800	14
HP0800	16
HP0800	18
HP0800	20
HP0800	22
HP0801	24
HP0801	26
HP0801	28
HP0887	30
HP0887	32
HP0887	34
HP0887	36
HP0887	38
HP0887	40
HP0887	42
HP0289	44
HP0289	46
HP0289	48
HP0289	50
HP0289	52
HP0289	54

HP0289	56
HP0289	58
HP0289	60
HP0289	62
HP0068	64
HP0068	66
HP0047	68
HP0047	70
HP0047	72
HP0069	74
HP0066	76
HP0268	78
HP1293	80
HP0061	82
HP0061	84
HP0061	86
HP0064	88
HP1198	90
HP1198	92
HP1198	94
HP1198	96
HP1198	98
HP1198	100
HP1198	102
HP1198	104
HP1198	106
HP1198	108
HP1198	110
HP1198	112
HP1198	114
HP1198	116

HP1198	118
	120
HP1231	
HP1032	122
HP1032	124
HP1032	. 126
HP1032	128
HP1032	130
HP1230	132
HP1230	134
HP1529	136
HP0978	138
HP0978	140
HP0071	142
HP0071	144
HP0071	146
HP0071	148
HP0071	150
HP0071	152
HP0073	154
HP0073	156
HP0073	158
HP0935	160
HP0935	162 · ·
HP0935	164
НР0338	166
HP0338	168
HP1246	170
HP1246	172
HP1246	174
HP1246	176
HP1246	178
111 12 10	

HP1246	180
HP1246	182
HP0797	184
HP0797	186
HP0797	188
HP0797	190
HP0797	192
HP0311	194
HP0067	196
HP0067	198
HP0067	200
HP0067	202
HP0067	204
HP1244	206
HP1244	208
HP1067	210
HP0875	212
HP0776	214
HP0776	216
HP0776	218
HP0776	220
HP0697	222
HP0697	224
HP0697	226
HP0697	228
HP0697	230
HP0697	232
HP0697	234
HP0697	236
HP0697	238
HP0697	240

НР0887	242
HP0887	244
HP0887	246
HP0887	248
HP1247	250
HP1247	252
HP0874	254
HP0072	256
HP0391	258
HP0391	260
НР0070	262
HP0070	264
HP0691	266
HP0691	268
HP1198	270
HP1198	272
	274
	276
HP0073 HP0073	

Table III:

Bait polypeptides	SID ®
(ORF reference according to Tomb et al.)	Nucleic acid sequence (SEQ ID N°)
HP0868	1
HP0868	3
HP0868	5
HP0868	7
HP0800	9
, HP0800	11
HP0800	13
HP0800	15
HP0800	17
HP0800	19
HP0800	21
HP0801	23
HP0801	25
HP0801	27
HP0887	29
HP0887	31
HP0887	33
HP0887	35
HP0887	37
HP0887	39
HP0887	41
HP0289	43
HP0289	45
HP0289	47
HP0289	49
HP0289	51
HP0289	53

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HP0289	55
HP0289	57
HP0289	59
HP0289	61
HP0068	63
HP0068	65
HP0047	67
HP0047	69
HP0047	71
HP0069	73
HP0066	75
HP0268	77
HP1293	79
НР0061	81
HP0061	83
HP0061	85
HP0064	87
HP1198	89
HP1198	91
HP1198	93
HP1198	95
HP1198	97
HP1198	99
HP1198	101
HP1198	103
HP1198	105
HP1198	107
HP1198	109
HP1198	111
HP1198	113
HP1198	115
	<u> </u>

HP1198	117
HP1231	119
HP1032	121
HP1032	123
HP1032	125
HP1032	127
HP1032	129
HP1230	131
HP1230	133
HP1529	135
HP0978	137
HP0978	139
HP0071	141
HP0071	143
HP0071	145
HP0071	147
HP0071	149
HP0071	151
HP0073	153
HP0073	155
HP0073	157
HP0935	159
HP0935	161
HP0935	163
HP0338	165
HP0338	167
HP1246	169
HP1246	171
HP1246	173
HP1246	175
HP1246	177

HP1246	179
HP1246	181
HP0797	183
HP0797	185
HP0797	187
HP0797	189
HP0797	191
HP0311	193
HP0067	195
HP0067	197
HP0067	199
HP0067	201
HP0067	203
HP1244	205
HP1244	207
HP1067	209
HP0875	211
HP0776	213
HP0776	215
HP0776	217
HP0776	219
HP0697	221
HP0697	223
HP0697	225
HP0697	227
НР0697	229
HP0697	231
HP0697	233
HP0697	235
HP0697	237
HP0697	239

HP0887	241
HP0887	243
HP0887	245
HP0887	247
HP1247	249
HP1247	251
HP0874	253
HP0072	255
	257
HP0391	259
HP0391	
HP0070	201
HP0070	263
HP0691	265
HP0691	267
HP1198	269
HP1198	271
HP0073	273
HP0073	275
HP0073	277
	<u> </u>

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Claims

- 1. A method for producing a collection of recombinant cell clones usable for two-hybrid systems comprising the steps of:
- 5 a) fragmenting DNA;
 - b) inserting polynucleotidic fragments obtained in step a) in plasmids in such a way that the expression of said plasmids in host cell leads to an hybrid polypeptide containing a specific domain capable of activating a reporter gene when associated with a complementary domain;
- 10 c) transforming cell clones with plasmids obtained in step b); and
 - d) optionally, selecting the transformed recombinant cell clones obtained in step c); wherein DNA of step a) is genomic DNA obtained from a prokaryotic micro-organism.
 - 2. A method according to claim 1, wherein the step a) of fragmenting DNA is carried by a nebulization process.
- 3. A method according to claim 1 or 2, wherein the prokaryotic microorganism is *Helicobacter pylori*.
 - 4. A method according claim 1 or 2, wherein the prokaryotic micro-organism is Staphylococcus aureus.
 - 5. A method according claim 1 or 2, wherein the prokaryotic micro-organism is Streptococcus pneumoniae.
 - 6. A method according claim 1 or 2, wherein the prokaryotic micro-organism is Escherichia coli.
 - 7. Collection of recombinant cell clones usable for two-hybrid systems obtainable by a method according to anyone of claims 1 to 6.
 - 8. Collection of recombinant cell clones usable for two-hybrid systems, each recombinant cell clone containing a polynucleotide inserted in a plasmid whose expression leads to hybrid polypeptide containing a specific domain, wherein the said polynucleotide is a genomic DNA fragment obtained from a prokaryotic microorganism.
- 9. Collection of recombinant cell clones usable for two-hybrid systems according to claim 8 wherein said genomic DNA fragment is obtained by a fragmentation process by nebulization.

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- 10. Collection of recombinant cell clones according to anyone of claims 7 to 9, wherein the prokaryotic micro-organism is *Helicobacter pylori*.
- 11. Collection of recombinant cell clones according to anyone of claims 7 to 9, wherein the prokaryotic micro-organism is Staphylococcus aureus.
- 12. Collection of recombinant cell clones according to anyone of claims 7 to 9, wherein the prokaryotic micro-organism is Streptococcus pneumoniae.
- 13. Collection of recombinant cell clones according to anyone of claims 7 to 9, wherein the prokaryotic micro-organism is *Escherichia coli*.
- 14. Collection of recombinant cell clones according to anyone of claims 7 to
 13, wherein the recombinant cell clones are selected from the group consisting of
 Gram+ or Gram- bacteria, yeasts, fungi and mammalian cells.
 - 15. Collection of recombinant cell clones according to claim 14, wherein the recombinant cell clones are selected from the group consisting of *Escherichia coli* bacteria and *Saccharomyces cerevisiae* yeast.
 - 16. Collection of recombinant cell clones according to claim 15, wherein the recombinant cell clones are *E. coli* bacteria.
 - 17. Collection of recombinant cell clones according to anyone of claims 7 to 16, wherein the plasmids comprise at least a nucleic sequence coding a promoter, a specific domain, a multicloning site where the said polypeptide is cloned, and a selection marker.
 - 18. Collection of recombinant cell clones according to anyone of claims 7 to 17, wherein the polynucleotide is inserted in the plasmid pACTIIst or pP6.
 - 19. Collection of recombinant cell clones according to claim 18, wherein the collection contains 10⁶ to 10⁷ recombinant *Escherichia coli* clones and wherein the proportion of different cell clones with insert is at least 60 %.
 - 20. Collection of recombinant cell clones according to claim 18 or 19 filed with CNCM on April 13, 1999 under number I-2181.
 - 21. Collection of recombinant cell clones according to claim 18 or 19 filed with CNCM on March 23, 2000 under number I-2416.
 - 22. Collection of recombinant cell clones according to claim 18 or 19 filed with CNCM on March 23, 2000 under number I-2414.

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- 23. Collection of recombinant cell clones according to claim 18 or 19 filed with CNCM on March 23, 2000 under number I-2415.
- 24. Collection of recombinant cell clones according to claim 18 or 19 filed with CNCM on March 23, 2000 under number I-2417.
- 25. Collection of recombinant cell clones according to claim 18, wherein the collection contains 10⁵ to 1.5 x 10⁶ haploid recombinant Saccharomyces cerevisiae clones and wherein the proportion of different cell clones with insert is at least 60 %.
- 26. Collection of recombinant cell clones according to claim 18 or 25 filed with CNCM on April 13, 1999 under number I-2182.
- 27. Collection of recombinant cell clones according to claim 18 or 25 filed with CNCM on March 23, 2000 under number I-2420.
- 28. Collection of recombinant cell clones according to claim 18 or 25 filed with CNCM on March 23, 2000 under number I-2419.
- 29. Collection of recombinant cell clones according to claim 18 or 25 filed with CNCM on March 23, 2000 under number I-2418.
 - 30. Collection of recombinant cell clones according to anyone of claims 7 to
 17, wherein the polynucleotide is inserted in the plasmid pAS2ΔΔ.
 - 31. Collection of recombinant cell clones according to anyone of claims 7 to 17, wherein the polynucleotide is inserted in a plasmid selected from the group consisting of pT25, pKT25, pUT18 and pUT18C.
 - 32. Kit for screening protein-protein interaction comprising a collection of recombinant cell clones usable for two-hybrid systems according to anyone of claims 7 to 31.
- 33. A yeast two-hybrid system method for identifying a recombinant cell
 25 clone containing a prey polynucleotide encoding a prey polypeptide capable of interacting with a bait polypeptide comprising the steps of:
 - a) mating at least one first haploid recombinant cell clone of a collection of recombinant cell clones according to claim 25 or 26 transformed with a plasmid containing the prey polynucleotide to be assayed with a second haploid recombinant S. cerevisiae cell clone transformed with a plasmid containing a bait polynucleotide encoding said bait polypeptide;
 - b) cultivating diploid cell obtained in step a) on selective medium; and

- c) selecting recombinant cell clones capable of growing on selective medium.
- 34. A yeast two-hybrid system method for identifying a prey polynucleotide encoding a prey polypeptide capable of interacting with a bait polypeptide comprising the steps of:
- a) identifying a recombinant cell clone containing a prey polynucleotide encoding a prey polypeptide capable of interacting with a bait polypeptide according to claim 33; and
 - b) characterizing the prey polynucleotide contained in each recombinant cell clone selected in step a).
- 35. A bacterial two-hybrid system method for identifying a recombinant cell clone containing a prey polynucleotide encoding a prey polypeptide capable of interacting with a bait polypeptide comprising the steps of:
 - a) transforming bacterial cell clones with a plasmid containing a bait polynucleotide encoding said bait polypeptide;
- b) rescuing prey plasmids containing prey polynucleotides from the collection according to claims 7 to 31;
 - c) transforming the recombinant bacterial cell clones obtained in step a) with the plasmid rescued in step b);
 - d) cultivating bacterial recombinant cells obtained in step c) on selective medium;
- 20 e) selecting recombinant cell clones capable of growing on selective medium.
 - 36. A bacterial two-hybrid system method for identifying a prey polynucleotide encoding a prey polypeptide capable of interacting with a bait polypeptide comprising the steps of:
 - a) identifying a bacterial recombinant cell clone containing a prey polynucleotide encoding a prey polypeptide capable of interacting with a bait polypeptide according to claim 35; and
 - b) characterizing the prey polynucleotide contained in each recombinant cell clone selected in step a).
- 37. Method according to anyone of claims 33 to 36, wherein the bait polypeptide is a human polypeptide.
 - 38. Method according to anyone of claims 33 to 36, wherein the bait polypeptide is a *Helicobacter pylori* polypeptide.

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- 39. Method according to anyone of claims 33 to 36, wherein the bait polypeptide is a Staphylococcus aureus polypeptide.
- 40. Method according to anyone of claims 33 to 36, wherein the bait polypeptide is a Streptococcus pneumoniae polypeptide.
- 41. Method according to anyone of claims 33 to 36, wherein the bait polypeptide is a *Escherichia coli* polypeptide.
- 42. A recombinant diploid yeast cell obtained by step a) of the method according to claim 33.
- 43. A recombinant diploid yeast cell obtained by the method according to claim 33.
 - 44. A set of two purified or isolated polynucleotides consisting of a first polynucleotide, or fragment thereof, encoding a prey polypeptide capable of interacting with a bait polypeptide and a second polynucleotide, or a fragment thereof having at least 12 consecutive nucleotides, encoding said bait polypeptide wherein the prey polynucleotide is identified by a method according to anyone of claims 34 and 36.
 - 45. A set of two purified or isolated polypeptides encoded by the set of two polynucleotides according to claim 44.
 - 46. Protein-protein interaction wherein the two interacting proteins consist of a set of two polypeptides according to claim 45.
 - 47. Protein-protein interaction according to claim 46, wherein the set of two polypeptides consists of two *Helicobacter pylori* polypeptides.
 - 48. Protein-protein interaction according to claim 46, wherein the set of two polypeptides consists of two *Staphylococcus aureus* polypeptides.
 - 49. Protein-protein interaction according to claim 46, wherein the set of two polypeptides consists of two *Streptococcus pneumoniae* polypeptides.
 - 50. Protein-protein interaction according to claim 46, wherein the set of two polypeptides consists of two *Escherichia coli* polypeptides.
 - 51. Isolated complex comprising at least the two polypeptides encoded by the set of two polynucleotides according to claim 44.
- 52. Isolated complex according to claim 51, characterized in that said complex comprises at least a polypeptide encoded by the ORF HP1198 and a polypeptide encoded by the ORF HP1293.

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- 53. Isolated complex according to claim 51, characterized in that said complex comprises at least a polypeptide encoded by the ORF HP1198 and a polypeptide encoded by the ORF HP0088.
- 54. Isolated complex according to claim 51, characterized in that said complex comprises at least a polypeptide encoded by the ORF HP1198 and a polypeptide encoded by the ORF HP1032.
- 55. A computable readable medium having stored thereon protein-protein interactions according to claim 46 to 50.
- 56. A computable readable medium according to claim 55, wherein the protein-protein interactions stored thereon is stored in a form of a map.
 - 57. A computable readable medium according to claim 55 or 56, wherein the protein-protein interactions stored thereon are linked to annotated database through Internet.
 - 58. A method for identifying a polynucleotide encoding a selecting interacting domain (SID®) of a prey polypeptide of interest from a prokaryotic microorganism capable of interacting with a bait polypeptide comprising the steps of:
 - a) selecting from prey polynucleotides identifyied by a method according to claim 34 or 36 all prey polynucleotides encoding a polypeptide capable of interacting with said bait polypeptide and containing a nucleic acid fragment identical to a nucleic fragment of the polynucleotide encoding the prey polypeptide of interest;
 - b) determining the polynucleotide common to said all prey polynucleotides selected in step a); and
 - c) identifying the polynucleotide determining in step b) as being the polynucleotide encoding the selected interacting domain (SID®) of said prey polypeptide of interest.
 - 59. Purified or isolated polynucleotide encoding a selecting interacting domain (SID®) of a prey polypeptide of interest from a prokaryotic micro-organism capable of interacting with a bait polypeptide obtainable by a method according to claim 58.
- 60. Purified or isolated polynucleotide according to claim 59 selected from the group consisting of:
 - a) a polynucleotide encoding an amino acids sequence identified by the reference indicated in the right column "SID®" in table II;

- b) a polynucleotide having the sequence identified by the reference indicated in the right column "SID®" in table III;
- c) fragment having at least 12 consecutive nucleotides of polynucleotide of a) or b), complement thereof, and RNA corresponding to said polynucleotide; and
- d) a polynucleotide having at least 80 % identity degree after alignment to a nucleic acid sequence of a polynucleotide of a) or b).
 - 61. Purified or isolated polypeptide selected from the group consisting of:
 - a) a polypeptide having an amino acids sequence identified by the reference indicated in the right column "SID®" in table II, and fragment thereof having at least 5 consecutive amino acids; and
 - b) a polypeptide encoded by a polynucleotide according to claim 59 or 60.
 - 62. Use of a polynucleotide according to claim 60 as a primer for amplification.
- 63. Use of a polynucleotide according to claim 60 as a specific probe for detection.
 - 64. Cloning or expression vector containing a polynucleotide according to anyone of claims 59 and 60.
 - 65. Vector according to claim 64, wherein the vector is the plasmid pACTIIst, pAS2ΔΔ or pP6.
- 20 66. Vector according to claim 64, wherein the vector is the plasmid selected from the group consisting of pT25, pKT25, pUT18 and pUT18C.
 - 67. Vector according to claim 64, wherein the vector is self replicated.
 - 68. Vector according to claim 64 or 67, wherein the vector is a viral vector.
 - 69. Vector according to claim 68, wherein the vector is chosen between an adenovirus, AAV, a retrovirus, a proxivirus or an herpes virus.
 - 70. Vector according to anyone of claims 64 to 69 including elements allowing expression and/or secretion of said polynucleotide in a host cell.
 - 71. Host cell transformed with a vector according to anyone of claims 64 to 70.
- Host cell according to claim 71, wherein the host cell is a prokaryotic cell.

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- 73. Host cell according to claim 71, wherein the host cell is an eukaryotic cell.
- 74. Method for producing a polypeptide according to anyone of claims 45 and 61, comprising the steps of:
- a) cultivating a host cell according to anyone of claims 71 to 73 under conditions and in culture medium allowing the growth of said host cell and the expression of said polypeptide; and
 - b) recovering said polypeptide directly from the culture medium or from said cultivated cell obtained in step a).
 - 75. Purified or isolated polypeptide obtained by the method according to claim 74.
 - 76. A method for selecting an agent capable of modulating the proteinprotein interaction of a step of two polypeptides according to claim 45 comprising the steps of:
 - a) cultivating a recombinant cell clone containing a reporter gene expression of which is toxic for said recombinant cell clone and transformed with two plasmids wherein:
 - i) the first plasmid contains a nucleic construct comprising a nucleic sequence encoding a first hybrid polypeptide containing one of said two polypeptides and a DNA binding domain;
- ii) the second plasmid contains a nucleic construct comprising a nucleic sequence encoding a second hybrid polypeptide containing the second of said two polypeptides and an activating domain capable of activating said toxic reporter gene when the first and the second hybrid polypeptides are interacting;
 - on a selective medium containing the agent to be tested and allowing the growth of said recombinant cell clone when the toxic reporter gene is not activated; and
 - b) selecting agent which is capable of inhibiting the growth of the recombinant cell clone cultivated in step a).
 - 77. A method for selecting an agent capable of modulating the proteinprotein interaction of a set of two polypeptides according to claim 45 comprising the steps of:

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- a) cultivating a permeable recombinant cell clone containing a reporter gene expression
 of which is toxic for said recombinant cell clone and transformed with two plasmids
 wherein:
- i) the first plasmid contains a nucleic construct comprising a nucleic sequence encoding a first hybrid polypeptide containing one of said two polypeptides and the first domain of an enzyme;
 - ii) the second plasmid contains a nucleic construct comprising a nucleic sequence encoding a second hybrid polypeptide containing the second of said two polypeptides and the second part of said enzyme capable of activating said toxic reporter gene when the first and the second hybrid polypeptides are interacting, said interaction restoring the activity of the enzyme;

on a selective medium containing the agent to be tested and allowing the growth of said recombinant cell clone when the toxic reporter gene is not activated; and

- b) selecting agent which is capable of inhibiting the growth of the recombinant cell clone cultivated in step a).
- 78. A method according to claim 77, for selecting an agent capable of modulating the interaction between a polypeptide encoded by the ORF HP1198, or a fragment or homologuous polypeptide thereof, and a polypeptide encoded by the ORF HP1293, or a fragment or homologuous polypeptide thereof.
- 79. A method according to claim 77, for selecting an agent capable of modulating the interaction between a polypeptide encoded by the ORF HP1198, or a fragment or homologuous polypeptide thereof, and a polypeptide encoded by the ORF HP0088, or a fragment thereof or homologuous polypeptide thereof.
- 80. A method according to claim 77, for selecting an agent capable of modulating the interaction between a polypeptide encoded by the ORF HP1198, or a fragment or homologuous polypeptide thereof, and a polypeptide encoded by the ORF HP1032, or a fragment or homologuous polypeptide thereof.
 - 81. Modulator agent selected by the method according to claim 76 or 77.
- 82. Kit for screening a modulator agent comprising at least one recombinant transformed cell clone according to step a) of claim 76 or 77.
 - 83. Use of a polypeptide according to anyone of claims 45 and 61 for the modulation of *Helicobacter pylori*'s protein interaction.

- 84. Method for the production of monoclonal or polyclonal comprising the step of immunization of an animal or human organism with an immunogenic agent comprising a polypeptide according to anyone of claims 45 and 61, a vector according to anyone of claims 65 to 70 or a host cell according to anyone of claims 71 to 73.
 - 85. Antibody obtained by the method according to claim 84.
- 86. A pharmaceutical composition comprising a compound selected from the group consisting of:
- a) a polynucleotide according to anyone of claims 59 and 60;
- b) a polypeptide according to anyone of claims 45 and 61;
- 10 c) a vector according to anyone of claims 62 to 70;
 - d) a host cell according to anyone of claims 71 to 73;
 - e) a modulator agent according to claim 80; and
 - f) an antibody according to claim 85.
- 87. A pharmaceutical composition according to claim 86, wherein said composition is administered by any route such as intravenous route, intramuscular route, oral route, or mucosal route with an acceptable physiological carrier and/or adjuvant.

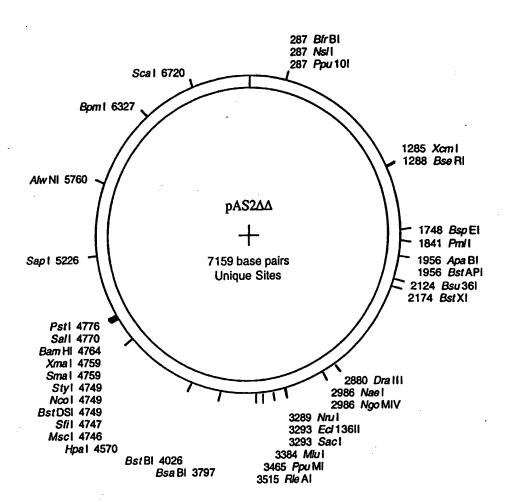


FIGURE 1

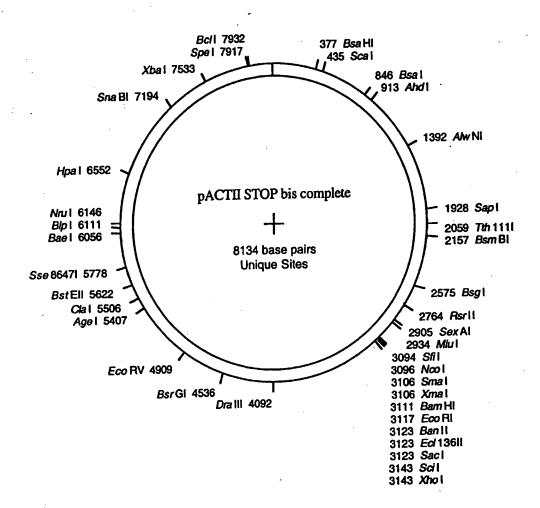
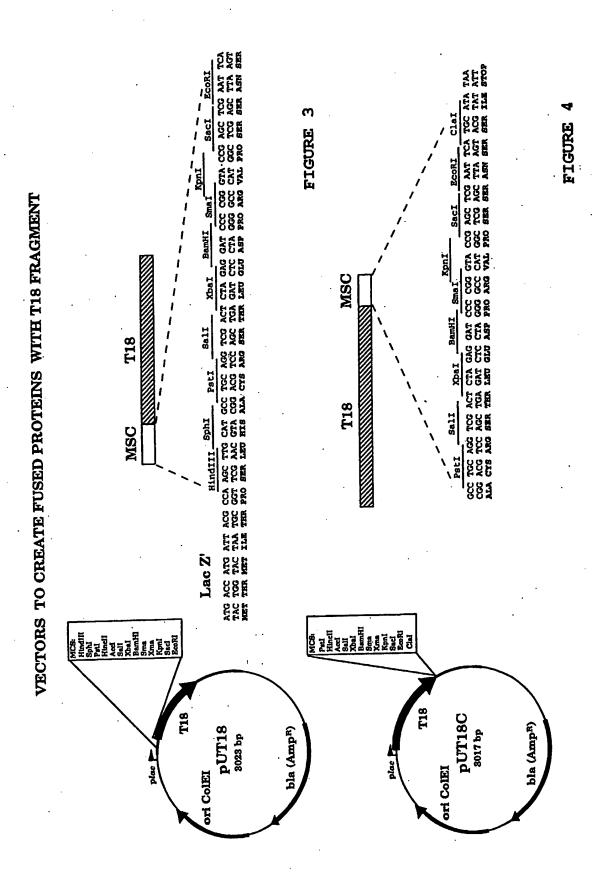
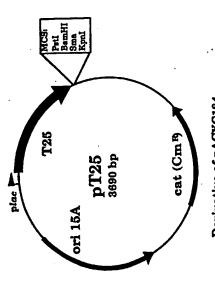


FIGURE 2



VECTORS TO CREATE FUSED PROTEINS WITH T25 FRAGMENT

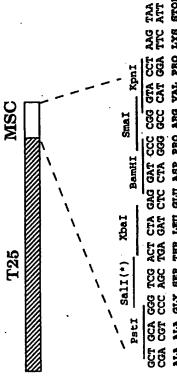


Derivative of pACYC184

ALA ALA GLY SER THR LEU GLU ASP PRO ARG VAL PRO LYS STOP GCT GCA GGG TCG ACT CTA GAG GAT CCC CGG GTA CCT AAG TAA CGA CGT CCC AGC TGA GAT CTC CTA GGG GCC CAT GGA TTC ATT MSC Smai BamHI Sali(*) Xbai(*) **T25** PstI

(*) Restriction sites are not unique

ល FIGURE



T25

pKT25 342 bp

ori 15A

ALA ALA GLY BER THR LEU GLU ASP PRO ARG VAL PRO LYS STOP

(*) Restriction site is not unique

Derivative of pSU40

kan (Km^R)

FIGURE

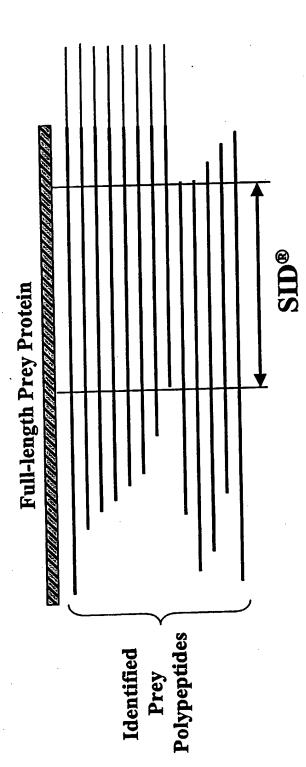


FIGURE 7

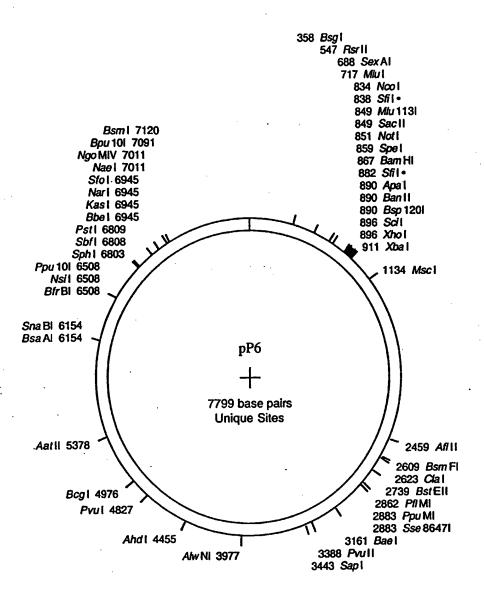


FIGURE 8

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<151> 1999-04-30
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                                                                    96
Ala Glu Glu Val Gly Leu Ser Leu Asp Lys Val Lys Asn Val Ile Lys
                                  25
gtg act aaa gag cet atc agt ttg gaa acc cca gtc ggc aat gat gat
                                                                    144
Val Thr Lys Glu Pro Ile Ser Leu Glu Thr Pro Val Gly Asn Ásp Ásp
                              40
          35
gat ggc aag ttt ggg gat ttc gtg gaa gat aag aat atc gtc agc tcc
                                                                    192
Asp Gly Lys Phe Gly Asp Phe Val Glu Asp Lys Asn Ile Val Ser Ser
                          55
att gat cac atc atg cga gaa gat ttg aaa gca caa att gaa agc gtt
                                                                    240
 Ile Asp His Ile Met Arg Glu Asp Leu Lys Ala Gln Ile Glu Ser Val
                                          75
                      70
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                                                                    288
 Leu Asp Gln Leu Asn Glu Arg Glu Lys Ala Val Ile Arg Met Arg Phe
                                      90
                  85
 ggg ctt tta gac gat gaa agc gat cga act tta gaa gaa att ggc aag
 Gly Leu Leu Asp Asp Glu Ser Asp Arg Thr Leu Glu Glu Ile Gly Lys
                                 105
 gaa ttg aat gtt act aga gaa agg gtg cgc cag att gaa agc tct gcg
             100
                                                                    384
 Glu Leu Asn Val Thr Arg Glu Arg Val Arg Gln Ile Glu Ser Ser Ala
                                                  125
                             120
 att aaa aaa ttg aga agc ccg cag tac ggg cgc att tta aga aac tat
                                                                     432
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                         135
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                                              60
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Ile Asp His Ile Met Arg Glu Asp Leu Lys Ala Gln Ile Glu Ser Val
                                         75
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Leu Asp Gln Leu Asn Glu Arg Glu Lys Ala Val Ile Arg Met Arg Phe
                                      90
Gly Leu Leu Asp Asp Glu Ser Asp Arg Thr Leu Glu Glu Ile Gly Lys
                                                    110
                                105
            100
Glu Leu Asn Val Thr Arg Glu Arg Val Arg Gln Ile Glu Ser Ser Ala
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                            120
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                                     10
                  5
gtt ggc tct atc act aaa atc aat ttt ttt cat aag cat ggg tat ttg
Val Gly Ser Ile Thr Lys Ile Asn Phe Phe His Lys His Gly Tyr Leu
                                 25
ggg att tat aaa aac cct ttt ttg aaa aat ggg gga gaa acg att tta
Gly Ile Tyr Lys Asn Pro Phe Leu Lys Asn Gly Gly Glu Thr Ile Leu
                             40
                                                  45
         35
aaa goo ttg gaa ttt atc got ttt gaa gag tto caa tta cat tot ttg
                                                                   192
Lys Ala Leu Glu Phe Ile Ala Phe Glu Glu Phe Gln Leu His Ser Leu
                                              60
                         55
cat tta gaa gtg atg gaa aac aat ttc aaa gcg atc gct ttt tat gaa
                                                                   240
His Leu Glu Val Met Glu Asn Asn Phe Lys Ala Ile Ala Phe Tyr Glu
                                          75
                     70
aaa aac cat tat gag tta gag ggg cgt ttg aaa ggc ttt att tct aaa
                                                                   288
Lys Asn His Tyr Glu Leu Glu Gly Arg Leu Lys Gly Phe Ile Ser Lys
                                      90
                 85
gat aag gag ttt ata gac gtt ctt ttg tat tat aag gat aag aaa gga
Asp Lys Glu Phe Ile Asp Val Leu Leu Tyr Tyr Lys Asp Lys Lys Gly
                                 105
                                                     110
            100
                                                                   363
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                             120
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                                  25
Gly Ile Tyr Lys Asn Pro Phe Leu Lys Asn Gly Gly Glu Thr Ile Leu
                              40
Lys Ala Leu Glu Phe Ile Ala Phe Glu Glu Phe Gln Leu His Ser Leu
                                              60
                          55
His Leu Glu Val Met Glu Asn Asn Phe Lys Ala Ile Ala Phe Tyr Glu
```

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65
Lys Asn His Tyr Glu Leu Glu Gly Arg Leu Lys Gly Phe Ile Ser Lys
                                     90
                 85
Asp Lys Glu Phe Ile Asp Val Leu Leu Tyr Tyr Lys Asp Lys Gly
                                105
            100
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Asn Ala Leu Asp Tyr Gly Val Cys Glu Lys Cys His Ser Lys Asn Val
                                      10
att atc act caa ggc aat gaa atg cgt ttg ttg tct tta gaa atg tta
                                                                   96
Ile Ile Thr Gln Gly Asn Glu Met Arg Leu Leu Ser Leu Glu Met Leu
                                  25
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gcg gaa
Ala Glu
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Ala Glu
 <210> 7
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 Met Glu Asp Tyr Ala Ser Arg Thr Ala Gly Ala Leu Glu Arg Leu Asp
                                      10
 aag att gtt gaa aca gaa cag aag aat caa caa act aaa ttg gac aca
                                                                    96
 Lys Ile Val Glu Thr Glu Gln Lys Asn Gln Gln Thr Lys Leu Asp Thr
              20
 gaa aat ttg aaa ata att att gaa act ttg aga agt aaa atc aat ggg
                                                                    144
 Glu Asn Leu Lys Ile Ile Ile Glu Thr Leu Arg Ser Lys Ile Asn Gly
 aat cag caa aag atg ctt gat aaa agt aaa gaa atg agc aga aat ttt
                                                                    192
 Asn Gln Gln Lys Met Leu Asp Lys Ser Lys Glu Met Ser Arg Asn Phe
                          · 55
 aag ctt gat agc act aaa aac gag ata gac gca att aaa gat ttg att
                                                                    240
 Lys Leu Asp Ser Thr Lys Asn Glu Ile Asp Ala Ile Lys Asp Leu Ile
 aaa aag gct aat gag caa ata gcc aat tat aat gag atg ata aag gat
                                                                    288
 Lys Lys Ala Asn Glu Gln Ile Ala Asn Tyr Asn Glu Met Ile Lys Asp
                                      90
                  85
 att gaa aaa cag aaa aag agt tgt aag gaa caa act tgg aaa ttt cta
                                                                    336
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Ile Glu Lys Gln Lys Lys Ser Cys Lys Glu Gln Thr Trp Lys Phe Leu
                                105
            100
                                                                   384
gto aat gaa ttt aaa agt gat ata caa gaa tat aat aaa aag tat tgo
Val Asn Glu Phe Lys Ser Asp Ile Gln Glu Tyr Asn Lys Lys Tyr Cys
                                                125
                            120
        115
ggt ttg gag aaa gga ata aac aat tta gag aaa gca att agt gaa aat
                                                                   432
Gly Leu Glu Lys Gly Ile Asn Asn Leu Glu Lys Ala Ile Ser Glu Asn
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                                                                   462
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Asn Gln Gln Lys Met Leu Asp Lys Ser Lys Glu Met Ser Arg Asn Phe
                         55
Lys Leu Asp Ser Thr Lys Asn Glu Ile Asp Ala Ile Lys Asp Leu Ile
                     70
Lys Lys Ala Asn Glu Gln Ile Ala Asn Tyr Asn Glu Met Ile Lys Asp
                                     90
                 85
Ile Glu Lys Gln Lys Lys Ser Cys Lys Glu Gln Thr Trp Lys Phe Leu
                                105
                                                    110
Val Asn Glu Phe Lys Ser Asp Ile Gln Glu Tyr Asn Lys Lys Tyr Cys
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                                                125
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                       135
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                                     10
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                                                                   96
Leu Gln Val Leu Glu Cys Glu Asn Cys Ser Met Thr Tyr Tyr Asp Arg
                                 25
                                                     30
            20
gat tat aat aga gaa tgt gag att tgc cct tat tgc gat gct aaa aaa
Asp Tyr Asn Arg Glu Cys Glu Ile Cys Pro Tyr Cys Asp Ala Lys Lys
                             40
cct gtc aga ctt gta gca aca agt tat tac caa aag agc gaa gtt ttt
                                                                   192
Pro Val Arg Leu Val Ala Thr Ser Tyr Tyr Gln Lys Ser Glu Val Phe
                                             60
                         55
tat ttt gtc tcg aat ttt aca gac cct att ttt tta ccg aca acc tta
                                                                   240
Tyr Phe Val Ser Asn Phe Thr Asp Pro Ile Phe Leu Pro Thr Thr Leu
                     70
                                         75
65
ttt aag ggg att gaa gtg gtt aaa agc gaa tgg gag ttt gca gag att
                                                                   288
Phe Lys Gly Ile Glu Val Val Lys Ser Glu Trp Glu Phe Ala Glu Ile
```

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85
                                      90
                                                                   336
gct aat aat ata ttg att ttt cat cat gac ata caa caa gaa aag att
Ala Asn Asn Ile Leù Ile Phe His His Asp Ile Gln Gln Glu Lys Ile
                                105
ctc att aat aat aaa aga ttg gat cac tat agg ata gaa ata gat tta
Leu Ile Asn Asn Lys Arg Leu Asp His Tyr Arg Ile Glu Ile Asp Leu
        115
                            120
gaa aaa gaa ttg act att tca tac aat ggt ttt tta att aag gtt caa
                                                                   432
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Pro Val Arg Leu Val Ala Thr Ser Tyr Tyr Gln Lys Ser Glu Val Phe
Tyr Phe Val Ser Asn Phe Thr Asp Pro Ile Phe Leu Pro Thr Thr Leu
Phe Lys Gly Ile Glu Val Val Lys Ser Glu Trp Glu Phe Ala Glu Ile
                                     90
Ala Asn Asn Ile Leu Ile Phe His His Asp Ile Gln Gln Glu Lys Ile
                                105
Leu Ile Asn Asn Lys Arg Leu Asp His Tyr Arg Ile Glu Ile Asp Leu
                            120
                                                125
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Lys Cys
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acg ctt ttt gtg atc ggg ttt atg agc tgc tcg gca agg ctg cct att
                                                                   96
Thr Leu Phe Val Ile Gly Phe Met Ser Cys Ser Ala Arg Leu Pro Ile
                                 25
tat gtg ctg ttt gta ggc tcg ttt ttc cct tct tca agt gct ggg ttt
Tyr. Val Leu Phe Val Gly Ser Phe Phe Pro Ser Ser Ser Ala Gly Phe
gtg ctg ttt tgc att tat att ttg ggg gcg gtt gtg gcg tta gtg atg
                                                                   192
Val Leu Phe Cys Ile Tyr Ile Leu Gly Ala Val Val Ala Leu Val Met
gcc aaa tta ctc aaa tta agc gtg ttt aaa gga caa acc gaa tct ttt
                                                                   240
Ala Lys Leu Leu Lys Leu Ser Val Phe Lys Gly Gln Thr Glu Ser Phe
65
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ttc	aat	atc	tac	200	aaa	tca	ctt	tct	tac	ctt	aaa	aag	gct	ggg	act	336
Phe	Ser	Ile	Tyr	Thr	Lys	Ser	Leu	Ser 105	Tyr	Leu	гÀг	гуѕ	110	GIÀ	1111	
		++=	~+~	aaa	aca	att	tta	atc	taa	ttt	atg	tct	caa	tac	cct	384
Tyr	Ile	Leu 115	Val	Gly	Ala	Ile	Leu 120	Ile	Trp	Phe	Met	Ser 125	Gln	Tyr	Pro	
		117	gcg	000	ata	222	act	tat	·aaa	caa	qaa	agc	ttg	tta	gtg	432
Lys	Ser 130	Asp	Ala	Ala	Met	Lys 135	Ala	Tyr	Lys	Gln	Glu 140	Ser	Leu	Leu	Val	
+		ant.	acc	act	ctt	tca	agc	gaa	gct	aaa	gaa	gaa	aaa	tta	aaa	480
Aar Aar	Luc	Den	Thr	Thr	Leu	Ser	Ser	Ğlu	Ala	Lys	Glu	Glu	Lys	Leu	Lys	
1 A E					150					122					100	
	tta	aaa	aca	gaa	ttq	gat	aaa	aag	aat	tta	aaa	aat	agc	att	gta	528
Glu	Leu	Lys	Thr	Glu 165	Leu	Asp	Lys	гÀг	170	Leu	ьys	ASII	Ser	175	Val	
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Gly	Arg	Gly	Gly	Ala	Tyr	Leu	GIU	Lуs 185	vaı	Pne	Ser	PLO	190	nap	1110	60.1
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Asp	Trp	Arg	Leu	Ser	Val	Ser	Leu 200	Val	Thr	GIĀ	rne	205	MIG	пÃ2	GIU	670
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Val	Val	Val	Ser	Thr	Leu	Gly 215	Val	Leu	Pne	Ser	220	GTÅ	Asp	GIII	Non	720
qaa	aaa	tct	gac	gct	ttt	aga	ggg	att	tta	aga	aaa	gaa	gtc	agc	gtg	120
Glu	Lys	Ser	Asp	Ala	Phe	Arg	Gly	Ile	Leu	Arg	гÀг	GIU	vaı	Ser	Val 240	
225					230					233					230	768
cct	agc	gga	atc	gct	ttt	atc	gtg	בככ	gtg	Mot	Dho	Tur	Tle	Pro	tgt Cvs	, 00
				245				•	250					255		816
ttt	gca	gcg	acc	att	act	TEE	ggt	agg	Glu	ycy Ala	Glu	Glv	Tle	Lvs	ttt Phe	
			260					265					210		Phe	864
gta	gcg	tat	tta	ttc	atc	CCC	aca mb-	acc Th≈	Val	Val	Δla	Tur	Ala	Phe	tcc	
		275	1				280					285	,		Ser	897
ttg	ata	gct	ttt	tat	gcg	act	Caa	Tlo	Leu	. Val						
	290	+	Phe	Tyr	Ala	295	GIII	116	пец	· ·						
	0> 1					•							•			
	1> 2															
	2> P			.+.~	nul c	ri										
		_	obac	cer	pyrc	-										
Ala		Met	. Ala	Thr 5		Thr	Leu	Gln	Asn 10	Туг	Asr	Glu	Arg	Let 15	ı Ile	
Thr	Leu	Phe	Val	Ile	Gly	Phe	Met	Ser 25	Cys		Ala	Arç	Ley 30	Pro	Ile	
Туг	. Val		Phe	Val	. Gly	Ser	Phe 40	Phe	Pro	Ser	Ser	: Sei 45	: Ala	Gly	/ Phe	
	50	1	e Cys			5:	Leu	Gly			01	,			l Met	
60	Lys	Let			- 70	Sei	· Val			12)				r Phe 80	
Ile	e Met			85	Lys	Туз			90	,				٦.		
Phe	e Ser	: Ile	Tyr 100	Thi	Lys	Sei	. Lev	1 Ser 105	Туг	Lev	ı Ly:	s Lys	3 Ala 110	a Gly	y Thr	

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Lys Ser Asp Ala Ala Met Lys Ala Tyr Lys Gln Glu Ser Leu Leu Val
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                        135
Asn Lys Asp Thr Thr Leu Ser Ser Glu Ala Lys Glu Glu Lys Leu Lys
                                        155
                    150
Glu Leu Lys Thr Glu Leu Asp Lys Lys Asn Leu Lys Asn Ser Ile Val
                                    170
                165
Gly Arg Gly Gly Ala Tyr Leu Glu Lys Val Phe Ser Pro Met Asp Phe
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Asp Trp Arg Leu Ser Val Ser Leu Val Thr Gly Phe Met Ala Lys Glu
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Val Val Val Ser Thr Leu Gly Val Leu Phe Ser Leu Gly Asp Gln Asn
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Glu Lys Ser Asp Ala Phe Arg Gly Ile Leu Arg Lys Glu Val Ser Val
                                         235
                    230
Pro Ser Gly Ile Ala Phe Ile Val Phe Val Met Phe Tyr Ile Pro Cys
                245
Phe Ala Ala Thr Ile Thr Phe Gly Arg Glu Ala Gly Gly Ile Lys Phe
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                                     10
gaa get tge geg aaa aac ttt gga geg ttt tgt gtg ttt gtg ggg att
Glu Ala Cys Ala Lys Asn Phe Gly Ala Phe Cys Val Phe Val Gly Ile
                                 25
gtg aga aaa gag gat aac att caa ggc ttg agt ttt gat att tat gaa
                                                                   144
Val Arg Lys Glu Asp Asn Ile Gln Gly Leu Ser Phe Asp Ile Tyr Glu
                             40
                                                 45
         35
gcg cta tta aag act tgg ttt gaa aaa tgg cac cat aaa gcc aaa gat
                                                                   192
Ala Leu Leu Lys Thr Trp Phe Glu Lys Trp His His Lys Ala Lys Asp
                                              60
                         55
ttg ggc gtg gtg tta aaa atg gcg cac agc ctg ggc gat gtt ttg ata
                                                                   240
Leu Gly Val Val Leu Lys Met Ala His Ser Leu Gly Asp Val Leu Ile
                                         75
                     70
gga caa agc tca ttt tta tgc gtt tca atg gga aag aat aga aaa aat
                                                                   288
Gly Gln Ser Ser Phe Leu Cys Val Ser Met Gly Lys Asn Arg Lys Asn
                                     90
gcc tta gaa cta tac gaa aat ttt att gaa gat ttt aag cat aac gct
                                                                   336
Ala Leu Glu Leu Tyr Glu Asn Phe Ile Glu Asp Phe Lys His Asn Ala
                                105
cct att tgg aaa tac gat tta atc cat aat aaa cgc att tat gct aaa
                                                                   384
Pro Ile Trp Lys Tyr Asp Leu Ile His Asn Lys Arg Ile Tyr Ala Lys
                            120
                                                                   423
gaa aga agc cac cct tta aaa ggg agc ggg ctt tta gct
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                        135
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Ala Leu Leu Lys Thr Trp Phe Glu Lys Trp His His Lys Ala Lys Asp
                         55
Leu Gly Val Val Leu Lys Met Ala His Ser Leu Gly Asp Val Leu Ile
                                         75
                     70
Gly Gln Ser Ser Phe Leu Cys Val Ser Met Gly Lys Asn Arg Lys Asn
                                     90
                 85
Ala Leu Glu Leu Tyr Glu Asn Phe Ile Glu Asp Phe Lys His Asn Ala
                                105
            100
Pro Ile Trp Lys Tyr Asp Leu Ile His Asn Lys Arg Ile Tyr Ala Lys
                                                 125
                            120
        115
Glu Arg Ser His Pro Leu Lys Gly Ser Gly Leu Leu Ala
                        135
  130
<210> 15
<211> 216
<212> DNA
<213> Helicobacter pylori
<220>
<221> CDS
<222> (1)..(216)
<400> 15
gta gaa gtg cga ttt ttt gga ccc ata aaa gaa gaa aat ttt ttc atc
Val Glu Val Arg Phe Phe Gly Pro Ile Lys Glu Glu Asn Phe Phe Ile
                                     10
aaa gcg aat gat ttg aag gaa tta aga gcg att tta caa gaa aaa gag
Lys Ala Asn Asp Leu Lys Glu Leu Arg Ala Ile Leu Gln Glu Lys Glu
                                  25
             20
ggc tta aaa gag tgg ttg ggc gtt tgc gcg ata gcc ctt aat gat cat
Gly Leu Lys Glu Trp Leu Gly Val Cys Ala Ile Ala Leu Asn Asp His
                             40
         35
 tta ata gac aat tta aac acg cct tta aaa gat ggc gat gta ata agt
                                                                    192
Leu Ile Asp Asn Leu Asn Thr Pro Leu Lys Asp Gly Asp Val Ile Ser
                                              60
                         55
     50
                                                                    216
 ttg ttg cca ccg gtt tgt ggg ggc
 Leu Leu Pro Pro Val Cys Gly Gly
 65
 <210> 16
 <211> 72
 <212> PRT
 <213> Helicobacter pylori
 <400> 16
 Val Glu Val Arg Phe Phe Gly Pro Ile Lys Glu Glu Asn Phe Phe Ile
                                      10
 Lys Ala Asn Asp Leu Lys Glu Leu Arg Ala Ile Leu Gln Glu Lys Glu
              20
 Gly Leu Lys Glu Trp Leu Gly Val Cys Ala Ile Ala Leu Asn Asp His
                                                  45
                              40
 Leu Ile Asp Asn Leu Asn Thr Pro Leu Lys Asp Gly Asp Val Ile Ser
                          55
 Leu Leu Pro Pro Val Cys Gly Gly
 <210> 17
 <211> 156
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<212> DNA
<213> Helicobacter pylori
<220>
<221> CDS
<222> (1)..(156)
<400> 17
aac gag caa aaa cag caa ttg att gaa ggg gtt tca gat ttg atg gtt
                                                                   48
Asn Glu Gln Lys Gln Gln Leu Ile Glu Gly Val Ser Asp Leu Met Val
aag gtg ctg aat aaa aat aag gct tct att gtg gtc att ata gat gag
                                                                    96
Lys Val Leu Asn Lys Asn Lys Ala Ser Ile Val Val Ile Ile Asp Glu
                                  25
             20
gtc gat tct aat aat tat ggt ctt ggg ggc gag agc gtc cat cat ttg
                                                                    144
Val Asp Ser Asn Asn Tyr Gly Leu Gly Gly Glu Ser Val His His Leu
                              40
         35
                                                                    156
agg caa aaa aac
Arg Gln Lys Asn
     50
<210> 18
<211> 52
<212> PRT
<213> Helicobacter pylori
Asn Glu Gln Lys Gln Gln Leu Ile Glu Gly Val Ser Asp Leu Met Val
<400> 18
                                      10
  1
Lys Val Leu Asn Lys Asn Lys Ala Ser Ile Val Val Ile Ile Asp Glu
                                                      30
                                  25
             20
Val Asp Ser Asn Asn Tyr Gly Leu Gly Gly Glu Ser Val His His Leu
                              40
         35
Arg Gln Lys Asn
     50
 <210> 19
 <211> 600
 <212> DNA
 <213> Helicobacter pylori
 <220>
 <221> CDS
 <222> (1)..(600)
 <400> 19
 att tat gcg cct att tta gcc ggg ctt gcc tct aat aac aaa tac tct
 Ile Tyr Ala Pro Ile Leu Ala Gly Leu Ala Ser Asn Asn Lys Tyr Ser
                                      10
   1
 tta att ggc tcc gca aga gcg acg atc caa ctg ctc agc ttt gaa gtg
                                                                    96
 Leu Ile Gly Ser Ala Arg Ala Thr Ile Gln Leu Leu Ser Phe Glu Val
                                  25
 gtc agc act tta acc att cta gcc ccc tta atg gtg gta gga tcg ctc
 Val Ser Thr Leu Thr Ile Leu Ala Pro Leu Met Val Val Gly Ser Leu
                                                   45
                              40
          35
 tot tta gtg gaa atc aat cat tac caa agc ggt ggg ttt tta gac tgg
                                                                     192
 Ser Leu Val Glu Ile Asn His Tyr Gln Ser Gly Gly Phe Leu Asp Trp
                                               60
                          55
 ctt gtg ttt aag cag cct cta gcg ttt gtt ttg ttt ttg atc gca agt
                                                                     240
 Leu Val Phe Lys Gln Pro Leu Ala Phe Val Leu Phe Leu Ile Ala Ser
                      70
  65
 tat gcc gaa ttg aat cga acc ccc ttt gac ttg cta gag cat gaa gcc
                                                                     288
 Tyr Ala Glu Leu Asn Arg Thr Pro Phe Asp Leu Leu Glu His Glu Ala
                                       90
                  85
 gag atc gtg gcg ggg tat tgc acc gaa tac agc ggc ttg aaa tgg ggc
                                                                     336
 Glu Ile Val Ala Gly Tyr Cys Thr Glu Tyr Ser Gly Leu Lys Trp Gly
                                                      110
                                 105
 atg ttc ttt tta gcg gaa tac gcg cat tta ttc gct ttt tct ttt gtg
                                                                     384
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Met Phe Phe Leu Ala Glu Tyr Ala His Leu Phe Ala Phe Ser Phe Val
                                                125
                            120
att tot att gtg ttt ttt ggc ggg ttt aac gca tgg ggc ttt atc cct
                                                                   432
Ile Ser Ile Val Phe Phe Gly Gly Phe Asn Ala Trp Gly Phe Ile Pro
                                            140
                        135
gga ggc ata gcg att ttg att aaa gcg ggc ttt ttt gtc ttt tta tcc
Gly Gly Ile Ala Ile Leu Ile Lys Ala Gly Phe Phe Val Phe Leu Ser
                                        155
                    150
atg tgg gtt aga gcg act tat ccg cat gtg cgc cca gac caa ctg atg
                                                                   528
Met Trp Val Arg Ala Thr Tyr Pro His Val Arg Pro Asp Gln Leu Met
                                    170
                165
gat atg tgc tgg aaa atc atg ctg cct tta gcg tta ttg aac att gtg
Asp Met Cys Trp Lys Ile Met Leu Pro Leu Ala Leu Leu Asn Ile Val
                                185
            180
cta acg ggc att atc att tta att
                                                                   600
Leu Thr Gly Ile Ile Ile Leu Ile
        195
<210> 20
<211> 200
<212> PRT
<213> Helicobacter pylori
Ile Tyr Ala Pro Ile Leu Ala Gly Leu Ala Ser Asn Asn Lys Tyr Ser
                                     10
Leu Ile Gly Ser Ala Arg Ala Thr Ile Gln Leu Leu Ser Phe Glu Val
                                 25
            20
Val Ser Thr Leu Thr Ile Leu Ala Pro Leu Met Val Val Gly Ser Leu
        35
                             40
Ser Leu Val Glu Ile Asn His Tyr Gln Ser Gly Gly Phe Leu Asp Trp
                         55
Leu Val Phe Lys Gln Pro Leu Ala Phe Val Leu Phe Leu Ile Ala Ser
                                         75
                     70
Tyr Ala Glu Leu Asn Arg Thr Pro Phe Asp Leu Leu Glu His Glu Ala
                                     90
                 85
Glu Ile Val Ala Gly Tyr Cys Thr Glu Tyr Ser Gly Leu Lys Trp Gly
                                                    110
                                105
Met Phe Phe Leu Ala Glu Tyr Ala His Leu Phe Ala Phe Ser Phe Val
                            120
                                                125
Ile Ser Ile Val Phe Phe Gly Gly Phe Asn Ala Trp Gly Phe Ile Pro
                                            140
    130
                        135
Gly Gly Ile Ala Ile Leu Ile Lys Ala Gly Phe Phe Val Phe Leu Ser
                                        155
                    150
Met Trp Val Arg Ala Thr Tyr Pro His Val Arg Pro Asp Gln Leu Met
                                    170
                165
Asp Met Cys Trp Lys Ile Met Leu Pro Leu Ala Leu Leu Asn Ile Val
                                185
            180
Leu Thr Gly Ile Ile Leu Ile
       195
                            200
<210> 21
<211> 474
<212> DNA
<213> Helicobacter pylori
<220>
<221> CDS
<222> (1)..(474)
<400> 21
gac gcc aag gct caa gaa gtg gcg atg tgc gta gcg atg ggt aaa acc
Asp Ala Lys Ala Gln Glu Val Ala Met Cys Val Ala Met Gly Lys Thr
                                     10
                 5
 1
cta aac gat aag ggg cgc ttg aaa cac tcc gtg cat gag ttt tac att
Leu Asn Asp Lys Gly Arg Leu Lys His Ser Val His Glu Phe Tyr Ile
```

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30
                                 25
aaa too coo gaa gaa atg goa aag oto ttt goa gat att ooa gaa got
                                                                   144
Lys Ser Pro Glu Glu Met Ala Lys Leu Phe Ala Asp Ile Pro Glu Ala
                             40
tta gaa aac acc caa gaa atc gct gat aaa tgc gtt tta gag att gat
                                                                   192
Leu Glu Asn Thr Gln Glu Ile Ala Asp Lys Cys Val Leu Glu Ile Asp
                                             60
                         55
tta aaa gac gat aaa aag aac ccc cca acc ccc cca agc ttc aaa ttc
                                                                   240
Leu Lys Asp Asp Lys Lys Asn Pro Pro Thr Pro Pro Ser Phe Lys Phe
                     70
act aaa got tac got caa aat gag ggg ctg aat ttt gaa gat gac got
                                                                   288
Thr Lys Ala Tyr Ala Gln Asn Glu Gly Leu Asn Phe Glu Asp Asp Ala
                                     90
                 85
tot tat tit goo tat aag got aga gaa ggo tig aaa gag ogo tia git
Ser Tyr Phe Ala Tyr Lys Ala Arg Glu Gly Leu Lys Glu Arg Leu Val
                                                     110
                                105
            100
tta gta cca aaa gaa aag cat gat caa tat aaa gag cgc cta gaa aaa
Leu Val Pro Lys Glu Lys His Asp Gln Tyr Lys Glu Arg Leu Glu Lys
                                                 125
                            120
        115
gaa att gaa gtc att acg aac atg aaa ttc cca ggg tat atg ctg att
Glu Ile Glu Val Ile Thr Asn Met Lys Phe Pro Gly Tyr Met Leu Ile
                                             140
                        135
gtg tgg gat ttt atc cgt tat gct aag gaa atg ggc att cct
Val Trp Asp Phe Ile Arg Tyr Ala Lys Glu Met Gly Ile Pro
                     150
 145
 <210> 22
 <211> 158
 <212> PRT
 <213> Helicobacter pylori
 Asp Ala Lys Ala Gln Glu Val Ala Met Cys Val Ala Met Gly Lys Thr
 <400> 22
                                      10
 Leu Asn Asp Lys Gly Arg Leu Lys His Ser Val His Glu Phe Tyr Ile
  1
 Lys Ser Pro Glu Glu Met Ala Lys Leu Phe Ala Asp Ile Pro Glu Ala
 Leu Glu Asn Thr Gln Glu Ile Ala Asp Lys Cys Val Leu Glu Ile Asp
 Leu Lys Asp Asp Lys Lys Asn Pro Pro Thr Pro Pro Ser Phe Lys Phe
                      70
  65
 Thr Lys Ala Tyr Ala Gln Asn Glu Gly Leu Asn Phe Glu Asp Asp Ala
 Ser Tyr Phe Ala Tyr Lys Ala Arg Glu Gly Leu Lys Glu Arg Leu Val
                                                     110
                                 105
 Leu Val Pro Lys Glu Lys His Asp Gln Tyr Lys Glu Arg Leu Glu Lys
                                                 125
                             120
 Glu Ile Glu Val Ile Thr Asn Met Lys Phe Pro Gly Tyr Met Leu Ile
                                             140
                         135
Val Trp Asp Phe Ile Arg Tyr Ala Lys Glu Met Gly Ile Pro
                                         155
                     150
 145
 <210> 23
 <211> 512
 <212> DNA
 <213> Helicobacter pylori
 <220>
 <221> CDS
 <222> (1)..(510)
 aag aat aaa gca ttc cac aac att gcc ctt gat att gaa acc cta aac
 Lys Asn Lys Ala Phe His Asn Ile Ala Leu Asp Ile Glu Thr Leu Asn
                                       10
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caa qaa gcc cta aaa aac act tat gat gtg agc gca atc agc ttt ggg
Gln Glu Ala Leu Lys Asn Thr Tyr Asp Val Ser Ala Ile Ser Phe Gly
                                  25
tta tac cct aaa att qcq aac qat tac gcc tta ctc ccc acg gca acq
Leu Tyr Pro Lys Ile Ala Asn Asp Tyr Ala Leu Leu Pro Thr Ala Thr
                             40
age ttt ggg aat gge tat ggg eet aaa tta gtg aaa aaa aag gge gtg
Ser Phe Gly Asn Gly Tyr Gly Pro Lys Leu Val Lys Lys Lys Gly Val
aaa ttq aaa aaa gat ttt aga gtc gca tta agt ggg gag cac acc acc
                                                                   240
Lys Leu Lys Lys Asp Phe Arg Val Ala Leu Ser Gly Glu His Thr Thr
                     70
                                         75
aac gcc ctc ttg ttt aag atc tat tac aaa cat gcg cgc atc act tat
                                                                   288
Asn Ala Leu Leu Phe Lys Ile Tyr Tyr Lys His Ala Arg Ile Thr Tyr
                 85
                                      90
atg aat ttt tta gac att gaa aaa gcg gtt ttg gaa gaa aaa gtg cat
                                                                   336
Met Asn Phe Leu Asp Ile Glu Lys Ala Val Leu Glu Glu Lys Val His
            100
                                105
gcg ggc gta ttg atc cat gag agt atc ttg gat ttt cat aat gaa tta
                                                                   384
Ala Gly Val Leu Ile His Glu Ser Ile Leu Asp Phe His Asn Glu Leu
        115
                            120
gaa gtg gaa aaa gaa ttg tgg gat gtt tgg aaa gaa ctc att gaa gtg
Glu Val Glu Lys Glu Leu Trp Asp Val Trp Lys Glu Leu Ile Glu Val
                        135
gat ttg ccc ttg cct tta ggg ggc atg gcg atc agg cga tct atc ccc
Asp Leu Pro Leu Pro Leu Gly Gly Met Ala Ile Arg Arg Ser Ile Pro
                    150
145
ttg tat cgc gcg att ttg att aaa aag gct tt
                                                                   512
Leu Tyr Arg Ala Ile Leu Ile Lys Lys Ala
                165
<210> 24
<211> 170
<212> PRT
<213> Helicobacter pylori
<400> 24
Lys Asn Lys Ala Phe His Asn Ile Ala Leu Asp Ile Glu Thr Leu Asn
Gln Glu Ala Leu Lys Asn Thr Tyr Asp Val Ser Ala Ile Ser Phe Gly
Leu Tyr Pro Lys Ile Ala Asn Asp Tyr Ala Leu Leu Pro Thr Ala Thr
Ser Phe Gly Asn Gly Tyr Gly Pro Lys Leu Val Lys Lys Gly Val
Lys Leu Lys Lys Asp Phe Arg Val Ala Leu Ser Gly Glu His Thr Thr
                     70
Asn Ala Leu Leu Phe Lys Ile Tyr Tyr Lys His Ala Arg Ile Thr Tyr
                                     90
Met Asn Phe Leu Asp Ile Glu Lys Ala Val Leu Glu Glu Lys Val His
                                105
            100
Ala Gly Val Leu Ile His Glu Ser Ile Leu Asp Phe His Asn Glu Leu
                            120
Glu Val Glu Lys Glu Leu Trp Asp Val Trp Lys Glu Leu Ile Glu Val
                                            140
    130
                        135
Asp Leu Pro Leu Pro Leu Gly Gly Met Ala Ile Arg Arg Ser Ile Pro
                   150
                                        155
Leu Tyr Arg Ala Ile Leu Ile Lys Lys Ala
               165
<210> 25
<211> 432
<212> DNA
<213> Helicobacter pylori
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336

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<220>
<221> CDS
<222> (1)..(432)
<400> 25
tta aaa atc att caa ggg gca tta gat act agg gag ctt tta aaa gcc
                                                                   48
Leu Lys Ile Ile Gln Gly Ala Leu Asp Thr Arg Glu Leu Leu Lys Ala
                                     10
                  5
tac caa gag gaa gct tgc gcg aaa aac ttt gga gcg ttt tgt gtg ttt
                                                                   96
Tyr Gln Glu Glu Ala Cys Ala Lys Asn Phe Gly Ala Phe Cys Val Phe
                                 25
             20
gtg ggg att gtg aga aaa gag gat aac att caa ggc ttg agt ttt gat
                                                                   144
Val Gly Ile Val Arg Lys Glu Asp Asn Ile Gln Gly Leu Ser Phe Asp
                             40
         35
att tat gaa gcg cta tta aag act tgg ttt gaa aaa tgg cac cat aaa
                                                                   192
Ile Tyr Glu Ala Leu Leu Lys Thr Trp Phe Glu Lys Trp His His Lys
                                             60
                         55
gcc aaa gat ttg ggc gtg gtg tta aaa atg gcg cac agc ctg ggc gat
Ala Lys Asp Leu Gly Val Val Leu Lys Met Ala His Ser Leu Gly Asp
                                         75
                     70
gtt ttg ata gga caa agc tca ttt tta tgc gtt tca atg gga aag aat
Val Leu Ile Gly Gln Ser Ser Phe Leu Cys Val Ser Met Gly Lys Asn
                                                          95
                                     90
                 85
aga aaa aat gcc tta gaa cta tac gaa aat ttt att gaa gat ttt aag
Arg Lys Asn Ala Leu Glu Leu Tyr Glu Asn Phe Ile Glu Asp Phe Lys
                                105
            100
cat aac gct cct att tgg aaa tac gat tta atc cat aat aaa cgc att
His Asn Ala Pro Ile Trp Lys Tyr Asp Leu Ile His Asn Lys Arg Ile
                                                 125
                            120
        115
tat gct aaa gaa aga agc cac cct tta aaa ggg agc ggg ctt tta gct
Tyr Ala Lys Glu Arg Ser His Pro Leu Lys Gly Ser Gly Leu Leu Ala
                         135
    130
<210> 26
 <211> 144
 <212> PRT
 <213> Helicobacter pylori
 <400> 26
 Leu Lys Ile Ile Gln Gly Ala Leu Asp Thr Arg Glu Leu Leu Lys Ala
                                      10
 Tyr Gln Glu Glu Ala Cys Ala Lys Asn Phe Gly Ala Phe Cys Val Phe
  1
                                  25
              20
 Val Gly Ile Val Arg Lys Glu Asp Asn Ile Gln Gly Leu Ser Phe Asp
                              40
          35
 Ile Tyr Glu Ala Leu Leu Lys Thr Trp Phe Glu Lys Trp His His Lys
                          55
      50
 Ala Lys Asp Leu Gly Val Val Leu Lys Met Ala His Ser Leu Gly Asp
                      70 .
 Val Leu Ile Gly Gln Ser Ser Phe Leu Cys Val Ser Met Gly Lys Asn
                                      90
                  85
 Arg Lys Asn Ala Leu Glu Leu Tyr Glu Asn Phe Ile Glu Asp Phe Lys
                                 105
             100
 His Asn Ala Pro Ile Trp Lys Tyr Asp Leu Ile His Asn Lys Arg Ile
                                                 125
                             120
 Tyr Ala Lys Glu Arg Ser His Pro Leu Lys Gly Ser Gly Leu Leu Ala
                         135
     130
 <210> 27
 <211> 516
 <212> DNA
 <213> Helicobacter pylori
 <220>
 <221> CDS
 <222> (1)..(516)
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<400> 27 tta agc ttt agc gcg gat aaa ttc ttt aac agt gcg caa gcg ggc att Leu Ser Phe Ser Ala Asp Lys Phe Phe Asn Ser Ala Gln Ala Gly Ile att atg ggg caa aaa gaa cgg gtt gaa gcg tta aaa aac cac ccc ctt Ile Met Gly Gln Lys Glu Arg Val Glu Ala Leu Lys Asn His Pro Leu 25 20 tat aga gtt tta agg gtg ggt aaa atc acg ctc acc ttg ctt ttt tgc Tyr Arg Val Leu Arg Val Gly Lys Ile Thr Leu Thr Leu Leu Phe Cys 40 age cta aaa gca tgg ata aat cat caa gaa gac att aca atc cat gcg Ser Leu Lys Ala Trp Ile Asn His Gln Glu Asp Ile Thr Ile His Ala 50 tta ttg aac caa act aaa gac gca tta ttg caa aaa gcc ctc aaa ctc 240 Leu Leu Asn Gln Thr Lys Asp Ala Leu Leu Gln Lys Ala Leu Lys Leu 75 70 tac gct ctt tta aag cct tta gaa ttg aat gtg agc ata gcc tct agc 288 Tyr Ala Leu Leu Lys Pro Leu Glu Leu Asn Val Ser Ile Ala Ser Ser 85 90 336 ttt tct aaa ata ggg aat ttg ttt ggt agg gaa tta gaa tcc ttt tgc Phe Ser Lys Ile Gly Asn Leu Phe Gly Arg Glu Leu Glu Ser Phe Cys 105 gtg aaa atc cag ccc aaa aac acc cgt gct tta aat agt gag aaa ctt 384 Val Lys Ile Gln Pro Lys Asn Thr Arg Ala Leu Asn Ser Glu Lys Leu 120 125 115 tat tta aag ctt ttc caa aaa ggc gtt atc gca agg att tca tgc gaa 432 Tyr Leu Lys Leu Phe Gln Lys Gly Val Ile Ala Arg Ile Ser Cys Glu 135 140 ttc gtg tgc ttt gaa gtc ttt agc ttg aat gaa aaa gat ttt gaa aaa 480 Phe Val Cys Phe Glu Val Phe Ser Leu Asn Glu Lys Asp Phe Glu Lys 150 155 atc gct ctg gtt tta gaa gaa att ctt aat aaa gct 516 Ile Ala Leu Val Leu Glu Glu Ile Leu Asn Lys Ala 165 <210> 28 <211> 172 <212> PRT <213> Helicobacter pylori <400> 28 Leu Ser Phe Ser Ala Asp Lys Phe Phe Asn Ser Ala Gln Ala Gly Ile 10 Ile Met Gly Gln Lys Glu Arg Val Glu Ala Leu Lys Asn His Pro Leu 25 20 Tyr Arg Val Leu Arg Val Gly Lys Ile Thr Leu Thr Leu Leu Phe Cys 40 Ser Leu Lys Ala Trp Ile Asn His Gln Glu Asp Ile Thr Ile His Ala 55 Leu Leu Asn Gln Thr Lys Asp Ala Leu Leu Gln Lys Ala Leu Lys Leu 75 Tyr Ala Leu Leu Lys Pro Leu Glu Leu Asn Val Ser Ile Ala Ser Ser 90 Phe Ser Lys Ile Gly Asn Leu Phe Gly Arg Glu Leu Glu Ser Phe Cys 105 Val Lys Ile Gln Pro Lys Asn Thr Arg Ala Leu Asn Ser Glu Lys Leu 120 Tyr Leu Lys Leu Phe Gln Lys Gly Val Ile Ala Arg Ile Ser Cys Glu 135 140 Phe Val Cys Phe Glu Val Phe Ser Leu Asn Glu Lys Asp Phe Glu Lys 150 155 Ile Ala Leu Val Leu Glu Glu Ile Leu Asn Lys Ala

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<210> 29
<211> 444
<212> DNA
<213> Helicobacter pylori
<220>
<221> CDS
<222> (1) .. (444)
<400> 29
atc att act caa gct aga aag gct aat ggg gtg att gtt cta gcc tta
                                                                   48
Ile Ile Thr Gln Ala Arg Lys Ala Asn Gly Val Ile Val Leu Ala Leu
                                     10
caa gac att aac caa cta agc gaa gtg aga aac gct caa agc ttt ata
                                                                   96
Gln Asp Ile Asn Gln Leu Ser Glu Val Arg Asn Ala Gln Ser Phe Ile
                                 25
             20
aaa aat atg ggg caa ttg att ttg tat ccc caa aga aat att gat acc
Lys Asn Met Gly Gln Leu Ile Leu Tyr Pro Gln Arg Asn Ile Asp Thr
                              40
         35
aaa gat tta aac gat aaa ttt ggc att aga cta agc gat aca gaa aaa
                                                                   192
Lys Asp Leu Asn Asp Lys Phe Gly Ile Arg Leu Ser Asp Thr Glu Lys
                         55
cat ttt tta gaa aac acc gcc gtt aat gaa tac aaa gtc tta ctc aaa
                                                                   240
His Phe Leu Glu Asn Thr Ala Val Asn Glu Tyr Lys Val Leu Leu Lys
                     70
aac atg aat gat ggc tca tct aac att ata gat gtg agc cta agt tct
                                                                    288
Asn Met Asn Asp Gly Ser Ser Asn Ile Ile Asp Val Ser Leu Ser Ser
                                      90
                 85
ttg ggt aat tac cta caa atc ttt agc tct aat tct agc atg gta gaa
                                                                    336
Leu Gly Asn Tyr Leu Gln Ile Phe Ser Ser Asn Ser Ser Met Val Glu
                                 105
            100
cac att gat aat ctc att aag cat tac cct aaa act tgg cga gaa gtc
                                                                    384
His Ile Asp Asn Leu Ile Lys His Tyr Pro Lys Thr Trp Arg Glu Val
                                                 125
                             120
        115
ttt gtg agt aac aaa cac gaa aat ttt gat gac aaa aaa cac tta gaa
Phe Val Ser Asn Lys His Glu Asn Phe Asp Asp Lys Lys His Leu Glu
                         135
    130
                                                                    444
aaq gtg ctt aaa
Lys Val Leu Lys
145
<210> 30
 <211> 148
 <212> PRT
 <213> Helicobacter pylori
 <400> 30
Ile Ile Thr Gln Ala Arg Lys Ala Asn Gly Val Ile Val Leu Ala Leu
                                      10
Gln Asp Ile Asn Gln Leu Ser Glu Val Arg Asn Ala Gln Ser Phe Ile
                                  25
Lys Asn Met Gly Gln Leu Ile Leu Tyr Pro Gln Arg Asn Ile Asp Thr
 Lys Asp Leu Asn Asp Lys Phe Gly Ile Arg Leu Ser Asp Thr Glu Lys
                          55
 His Phe Leu Glu Asn Thr Ala Val Asn Glu Tyr Lys Val Leu Leu Lys
                                          75
                      70
 Asn Met Asn Asp Gly Ser Ser Asn Ile Ile Asp Val Ser Leu Ser Ser
                                      90
                  85
 Leu Gly Asn Tyr Leu Gln Ile Phe Ser Ser Asn Ser Ser Met Val Glu
                                 105
 His Ile Asp Asn Leu Ile Lys His Tyr Pro Lys Thr Trp Arg Glu Val
                                                 125
                            120
 Phe Val Ser Asn Lys His Glu Asn Phe Asp Asp Lys Lys His Leu Glu
                                             140
                         135
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Lys Val Leu Lys
145
<210> 31
<211> 426
<212> DNA
<213> Helicobacter pylori
<220>
<221> CDS
<222> (1)..(426)
<400> 31
acg gtg ggc gat gtt ttt ggt gaa aac ggg ctt tta aac gcg cta gat
Thr Val Gly Asp Val Phe Gly Glu Asn Gly Leu Leu Asn Ala Leu Asp
                                     .10
cct acg gaa aga aaa aat gat caa atg ctt tta gag caa atc caa
                                                                   96
Pro Thr Glu Arg Lys Lys Ile Asp Gln Met Leu Leu Glu Gln Ile Gln
                                 25
gcc cat tot toa ggg ttt gaa aaa tto ato gtg aaa act tta ggg att
                                                                   144
Ala His Ser Ser Gly Phe Glu Lys Phe Ile Val Lys Thr Leu Gly Ile
                             40
         35
gaa aat gta gag aat ttc atc aat aac tgg tat ggc aag caa agc ttg
                                                                   192
Glu Asn Val Glu Asn Phe Ile Asn Asn Trp Tyr Gly Lys Gln Ser Leu
                                              60
                         55
agt tot ttt gcc aat aat ttt gtg cot gga ggc ttg aat caa gcc ctt
                                                                   240
Ser Ser Phe Ala Asn Asn Phe Val Pro Gly Gly Leu Asn Gln Ala Leu
                                         75
                     70
gat aaa ata ggc tot agc tot gat gcc aaa gac tta cag aac ttc ttg
                                                                   288
Asp Lys Ile Gly Ser Ser Ser Asp Ala Lys Asp Leu Gln Asn Phe Leu
                                     90
                 85
gat aaa acg act ttt ggg gat att tta aat caa atg att gaa caa gcc
                                                                   336
Asp Lys Thr Thr Phe Gly Asp Ile Leu Asn Gln Met Ile Glu Gln Ala
                                                    110
                                105
            100
ccc tta atc aat aaa ctc att tct tgg ctg ggt ccg cag gat ttg agc
                                                                   384
Pro Leu Ile Asn Lys Leu Ile Ser Trp Leu Gly Pro Gln Asp Leu Ser
                                                 125
                            120
        115
gtt tta gtg aat atc gct tta aat agc atc act aac cct agt
                                                                   426
Val Leu Val Asn Ile Ala Leu Asn Ser Ile Thr Asn Pro Ser
    130
<210> 32
<211> 142
<212> PRT
<213> Helicobacter pylori
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Pro Thr Glu Arg Lys Lys Ile Asp Gln Met Leu Leu Glu Gln Ile Gln
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Ala His Ser Ser Gly Phe Glu Lys Phe Ile Val Lys Thr Leu Gly Ile
                              40
Glu Asn Val Glu Asn Phe Ile Asn Asn Trp Tyr Gly Lys Gln Ser Leu
                         55
                                              60
Ser Ser Phe Ala Asn Asn Phe Val Pro Gly Gly Leu Asn Gln Ala Leu
                                          75
Asp Lys Ile Gly Ser Ser Ser Asp Ala Lys Asp Leu Gln Asn Phe Leu
                                      90
                 85
Asp Lys Thr Thr Phe Gly Asp Ile Leu Asn Gln Met Ile Glu Gln Ala
                                                     110
                                105
            100
Pro Leu Ile Asn Lys Leu Ile Ser Trp Leu Gly Pro Gln Asp Leu Ser
                                                 125
                             120
        115
Val Leu Val Asn Ile Ala Leu Asn Ser Ile Thr Asn Pro Ser
    130
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<210> 33
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<213> Helicobacter pylori
<220>
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Gln Ala His His Leu Lys Asn Leu Leu Glu Ala Phe Tyr His Gln Asn
                                     10
aaa gag agt ttg ggc ttt ttt tcc cct tat ttt agt ttg cga tct caa
                                                                   96
Lys Glu Ser Leu Gly Phe Phe Ser Pro Tyr Phe Ser Leu Arg Ser Gln
                                 25
             20
acc cet age gte tet tat gaa age geg tta get tet tta gaa aac tat
Thr Pro Ser Val Ser Tyr Glu Ser Ala Leu Ala Ser Leu Glu Asn Tyr
                             40
         35
ttt atg get ttg tte caa tee cat ttt aaa gae gat aee gea ete caa
                                                                   192
Phe Met Ala Leu Phe Gln Ser His Phe Lys Asp Asp Thr Ala Leu Gln
                         55
cag aat ttt aaa gga ttg ttg caa gcc ttt gtt tct atg gct aaa gac
                                                                   240
Gln Asn Phe Lys Gly Leu Leu Gln Ala Phe Val Ser Met Ala Lys Asp
                                         75 '
                     70
aaa cga tcc caa atc gct ctt aac gcc caa gct aaa gac aac gcc aag
                                                                   288
Lys Arg Ser Gln Ile Ala Leu Asn Ala Gln Ala Lys Asp Asn Ala Lys
                                     90
                 85
cta act ttt aac gcc ttg tta gaa agc ctt agc gtg aat ttc ttt caa
                                                                   336
Leu Thr Phe Asn Ala Leu Leu Glu Ser Leu Ser Val Asn Phe Phe Gln
                                105
            100
                                                                   357
tct tac aaa ata agc cat gag
Ser Tyr Lys Ile Ser His Glu
        115
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Gln Ala His His Leu Lys Asn Leu Leu Glu Ala Phe Tyr His Gln Asn
                                      10
                  -5
Lys Glu Ser Leu Gly Phe Phe Ser Pro Tyr Phe Ser Leu Arg Ser Gln
                                  25
             20
Thr Pro Ser Val Ser Tyr Glu Ser Ala Leu Ala Ser Leu Glu Asn Tyr
                              40
         35
Phe Met Ala Leu Phe Gln Ser His Phe Lys Asp Asp Thr Ala Leu Gln
                          55
Gln Asn Phe Lys Gly Leu Leu Gln Ala Phe Val Ser Met Ala Lys Asp
                                         75
                      70
Lys Arg Ser Gln Ile Ala Leu Asn Ala Gln Ala Lys Asp Asn Ala Lys
                                      90
                  85
Leu Thr Phe Asn Ala Leu Leu Glu Ser Leu Ser Val Asn Phe Phe Gln
                                 105
             100
Ser Tyr Lys Ile Ser His Glu
        115
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<212> DNA
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<221> CDS
<222> (1)..(978)
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gtg ggt tot gga gcc ggg agg aaa gcc agc tot acg gtt tta act ttg
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PCT/IB00/00603 WO 00/66722 18

1	Gly			5					10					15		
caa	gct	tca	gaa	ggg	att	act	agc	agt	aaa	aat	gcg	gaa	att	tct	ctt	96
	Ala		20					25					30			
tat	gat	ggc	gcc	acg	ctc	aat	ttg	gct	tca	aac	agc	gtt	aaa	tta	atg	144
_	Asp	35					40					45				
ggt	aat	gtg	tgg	atg	ggc	cgt	ttg	caa	tat	gtg	gga	gcg	tat	ttg	gcc	192
_	Asn 50					55					60					
cct	tca	tac	agc	acg	ata	aac	act	tca	aaa	gtg	aca	ggg	gaa	gtg	aat	240
Pro 65	Ser	Tyr	Ser	Thr	70	ASN	Thr	Ser	rys	75	1111	GIY	GIU	Val	80	
ttt	aac	cat	ctc	act		ggc	gat	cac	aac		gct	caa	gca	ggc	att	288
Phe	Asn	His	Leu	Thr	Val	·Gĺy	Asp	His	Asn	Ala	Ala	Gln	Ala	Gly	Ile	
				85					90					95		226
atc	gct	agt	aac	aag	act	cat	att	ggc	aca	ctg	gat	ttg	Trn	Caa	agc	336
Ile	Ala	Ser	100	гÀг	THE	HIS	TTE	105	1111	теп	vsh	nen	110	GIII	261	
aca	gga	cta		att	atc	qcc	cct		gaa	ggc	ggt	tat		gat	aaa	384
Ala	Gly	Leu	Asn	Ile	Ile	Ala	Pro	Pro	Ğlu	Gly	Gly	Tyr	Lys	Asp	Lys	
	_	115					120					125				430
cct	aag	gat	aaa	cct	agt	aac	acc	acg	caa	aat	aat	gct	aac	aac	aac	432
Pro	Lys	Asp	Lys	Pro	Ser	135	Thr	Thr	GIN	ASN	140	WIG	ASII	ASII	Wâli	
caa	130 caa	aac	aαc	act	caa		aat	aqt	aac	act		gtt	att	aac	cca	480
Gln	Gln	Asn	Ser	Ala	Gln	Asn	Asn	Ser	Asn	Thr	Gln	Val	Ile	Asn	Pro	
145					150					155					160	
ccc	aat	agc	gcg	caa	aaa	aca	gaa	att	caa	CCC	acg	caa	gtc	att	gat	528
Pro	Asn	Ser	Ala	Gln 165	Lys	Thr	GIU	TIE	170	PIO	Thr	GIN	AGI	175	Asp	
aaa	cct	ttt	act		aac	aaa	gac	acq		gtc	aat	att	gat		atc	576
Glv	Pro	Phe	Ala	Gly	Gly	Lys	Asp	Thr	Val	Val	Asn	Ile	Āsp	Arg	Ile	
-			180					185					190			604
aac	act	aac	gct	gat	ggc	acg	att	aaa	gtg	gga	ggg	Tur	aaa	gct Ala	CCT	624
Asn	Thr	Asn 195	Ala	Asp	GIY	Thr	200	гÃа	Val	GIY	GIY	205	цуз	AIG.	261	
ctt	acc	acc	aat	aca	gct	cat	ttg	cat	atc	ggc	aaa	ggc	ggt	atc	aat	672
Leu	Thr	Thr	Asn	Ala	Ála	His	Leu	His	Ile	Gly	Lys	Gly	Gly	Ile	Asn	
	210					215					220					300
ctg	tcc Ser	aat	caa	gcg	agc	ggg	cgc	acc	ctt	tta	gtg	gaa	aat	Cta	acc Thr	720
Leu 225	Ser	Asn	GIN	ATA	230	GTA	Arg	TIII	neu	235	Val	GIU	no	Deu	240	
aaa	aat	atc	acc	att	gat	qqq	cct	tta	aga	gtg	aat	aat	caa	gtg	ggt	768
Gly	Asn	Ile	Thr	Val	Asp	Gly	Pro	Leu	Arg	Val	Asn	Asn	Gln	Val	Gly	
				245					250					255		016
ggt	tat	gct	ttg	gça	gga	tca	agc	gcg	aat	Dbo	gag	Dbo	aag	gct Nla	ggt	816
Gly	Tyr	Ala	Leu 260	Ala	GIĀ	Ser	Ser	265	ASII	rne	GIU	File	270	VIG	GIY	
200	gat	acc	200	aac	ggc	aca	acc		ttt	aat	aac	gat		agt	ttg	864
Thr	Asp	Thr	Lys	Asn	Gly	Thr	Ala	Thr	Phe	Asn	Asn	Asp	Ile	Ser	Leu	
	_	275					280					285				
gga	aga	ttt	gtg	aat	tta	aaa	gtg	gat	gct	cat	aca	gct	aat	ttt	aaa	912
Gly	Arg	Phe	Val	Asn	Leu		val	Asp	ATS	H1S	300	WIS	ASN	rne	гÀ2	
	290 att	~ ~+	20-	ga+	22+	295	aat	ttc	aac	acc		gat	ttt	aσt	gge	960
Glu	Ile	Asp	Thr	Glv	Asn	Glv	Glv	Phe	Asn	Thr	Leu	Asp	Phe	Ser	Gly	
305				~-,	310	,		-		315		•			320	
gtt	aca					at					•					980
Val	Thr	Gly	Lys	Val	Asn											

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<213> Helicobacter pylori
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Val Gly Ser Gly Ala Gly Arg Lys Ala Ser Ser Thr Val Leu Thr Leu
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Gln Ala Ser Glu Gly Ile Thr Ser Ser Lys Asn Ala Glu Ile Ser Leu
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            20
Tyr Asp Gly Ala Thr Leu Asn Leu Ala Ser Asn Ser Val Lys Leu Met
                             40
        35
Gly Asn Val Trp Met Gly Arg Leu Gln Tyr Val Gly Ala Tyr Leu Ala
                                            60
                        55
Pro Ser Tyr Ser Thr Ile Asn Thr Ser Lys Val Thr Gly Glu Val Asn
                                        75
                    70
Phe Asn His Leu Thr Val Gly Asp His Asn Ala Ala Gln Ala Gly Ile
                                    90
                 85
Ile Ala Ser Asn Lys Thr His Ile Gly Thr Leu Asp Leu Trp Gln Ser
                                                  110
                        . 105
            100
Ala Gly Leu Asn Ile Ile Ala Pro Pro Glu Gly Gly Tyr Lys Asp Lys
                                                125
                           120
Pro Lys Asp Lys Pro Ser Asn Thr Thr Gln Asn Asn Ala Asn Asn Asn
        115
                                            140
                       135
Gln Gln Asn Ser Ala Gln Asn Asn Ser Asn Thr Gln Val Ile Asn Pro
    130
                                        155
                   150
Pro Asn Ser Ala Gln Lys Thr Glu Ile Gln Pro Thr Gln Val Ile Asp
                                                        175
                                    170
Gly Pro Phe Ala Gly Gly Lys Asp Thr Val Val Asn Ile Asp Arg Ile
                165
                                                   190
                                185
           180
Asn Thr Asn Ala Asp Gly Thr Ile Lys Val Gly Gly Tyr Lys Ala Ser
                                                205
                            200
 . 195
Leu Thr Thr Asn Ala Ala His Leu His Ile Gly Lys Gly Gly Ile Asn
                                            220
                        215
Leu Ser Asn Gin Ala Ser Gly Arg Thr Leu Leu Val Glu Asn Leu Thr
                                       235
                    230
 Gly Asn Ile Thr Val Asp Gly Pro Leu Arg Val Asn Asn Gln Val Gly
                                    250
                245
 Gly Tyr Ala Leu Ala Gly Ser Ser Ala Asn Phe Glu Phe Lys Ala Gly
                                                   270
                                265
 Thr Asp Thr Lys Asn Gly Thr Ala Thr Phe Asn Asn Asp Ile Ser Leu
                                               285
                            280
         275
 Gly Arg Phe Val Asn Leu Lys Val Asp Ala His Thr Ala Asn Phe Lys
                                            300
                        295
 Gly Ile Asp Thr Gly Asn Gly Gly Phe Asn Thr Leu Asp Phe Ser Gly
                                        315
                   310
 Val Thr Gly Lys Val Asn
                 325
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 <222> (1)..(360)
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 Ser Asn Leu Cys Gly Asn Gly Ser Ser Gly Ser Ser Gly Thr Thr Cys
                                     10
 tee ggt tgg ett ate aac ett tta ggg gea ate eee aee aat gga gtg
 Ser Gly Trp Leu Ile Asn Leu Leu Gly Ala Ile Pro Thr Asn Gly Val
```

```
20
                                  25
age gat acg aat aat tta att aat etg etc act gaa tte att aaa acc
Ser Asp Thr Asn Asn Leu Ile Asn Leu Leu Thr Glu Phe Ile Lys Thr
                              40
gcc ggg ttt atc caa aat aat gat agt agt gta tct act agt ctt aca
                                                                   192
Ala Gly Phe Ile Gln Asn Asn Asp Ser Ser Val Ser Thr Ser Leu Thr
                         55
age get ttt caa gee att acg age get att tet caa ggg ttt caa gee
                                                                   240
Ser Ala Phe Gln Ala Ile Thr Ser Ala Ile Ser Gln Gly Phe Gln Ala
                     70
                                          75
tta caa aac gat att agc cct aat gcg att tta acc ttg ctc caa gag
                                                                   288
Leu Gln Asn Asp Ile Ser Pro Asn Ala Ile Leu Thr Leu Leu Gln Glu
                                      90.
                 85
att act tot aac acc acc act cag toa tto tog caa acc tta cgg
                                                                   336
Ile Thr Ser Asn Thr Thr Thr Ile Gln Ser Phe Ser Gln Thr Leu Arg
                                 105
            100
cag ctt tta ggg gat aaa aca ttc tt
                                                                   362
Gln Leu Leu Gly Asp Lys Thr Phe
        115
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<213> Helicobacter pylori
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Ser Asn Leu Cys Gly Asn Gly Ser Ser Gly Ser Ser Gly Thr Thr Cys
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Ser Gly Trp Leu Ile Asn Leu Leu Gly Ala Ile Pro Thr Asn Gly Val
                                 25
             20
Ser Asp Thr Asn Asn Leu Ile Asn Leu Leu Thr Glu Phe Ile Lys Thr
         35
                            . 40
Ala Gly Phe Ile Gln Asn Asn Asp Ser Ser Val Ser Thr Ser Leu Thr
                         55
                                              60
Ser Ala Phe Gln Ala Ile Thr Ser Ala Ile Ser Gln Gly Phe Gln Ala
                     70
                                          75
Leu Gln Asn Asp Ile Ser Pro Asn Ala Ile Leu Thr Leu Leu Gln Glu
                                     90
                 85
Ile Thr Ser Asn Thr Thr Thr Ile Gln Ser Phe Ser Gln Thr Leu Arg
                                105
            100
Gln Leu Leu Gly Asp Lys Thr Phe
        115
<210> 39
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<212> DNA
<213> Helicobacter pylori
<220>
<221> CDS
<222> (1)..(447)
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ctc ttt gca gat att cca gaa gct tta gaa aac acc caa gaa atc gct
                                                                   48
Leu Phe Ala Asp Ile Pro Glu Ala Leu Glu Asn Thr Gln Glu Ile Ala
                                     10
gat aaa tgc gtt tta gag att gat tta aaa gac gat aaa aag aac ccc
                                                                   96
Asp Lys Cys Val Leu Glu Ile Asp Leu Lys Asp Asp Lys Lys Asn Pro
            20
                                 25
cca acc ccc cca agc ttc aaa ttc act aaa gct tac gct caa aat gag
                                                                   144
Pro Thr Pro Pro Ser Phe Lys Phe Thr Lys Ala Tyr Ala Gln Asn Glu
        35
ggg ctg aat ttt gaa gat gac gct tct tat ttt gcc tat aag gct aga
                                                                   192
Gly Leu Asn Phe Glu Asp Asp Ala Ser Tyr Phe Ala Tyr Lys Ala Arg
gaa ggc ttg aaa gag cgc tta gtt tta gta cca aaa gaa aag cat gat
```

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Glu Gly Leu Lys Glu Arg Leu Val Leu Val Pro Lys Glu Lys His Asp
                                          75
                     70
caa tat aaa gag cgc cta gaa aaa gaa att gaa gtc att acg aac atg
                                                                   288
Gln Tyr Lys Glu Arg Leu Glu Lys Glu Ile Glu Val Ile Thr Asn Met
                                     90
                 85
aaa ttc cca ggg tat atg ctg att gtg tgg gat ttt atc cgt tat gct
Lys Phe Pro Gly Tyr Met Leu Ile Val Trp Asp Phe Ile Arg Tyr Ala
                                                     110
                                105
            100
aag gaa atg ggc att cet gta ggg cet ggt agg ggg agt geg gee ggg
                                                                   384
Lys Glu Met Gly Ile Pro Val Gly Pro Gly Arg Gly Ser Ala Ala Gly
                                                 125
                            120
        115
age ttg gtg get ttt get tta aaa ate acg gat att gae eet ttg aaa
                                                                    432
Ser Leu Val Ala Phe Ala Leu Lys Ile Thr Asp Ile Asp Pro Leu Lys
                        135
    130
                                                                    448
tac gat ttg ctc ttt g
Tyr Asp Leu Leu Phe
145
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<213> Helicobacter pylori
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Asp Lys Cys Val Leu Glu Ile Asp Leu Lys Asp Asp Lys Lys Asn Pro
             20
Pro Thr Pro Pro Ser Phe Lys Phe Thr Lys Ala Tyr Ala Gln Asn Glu
                                                  45.
         35
Gly Leu Asn Phe Glu Asp Asp Ala Ser Tyr Phe Ala Tyr Lys Ala Arg
                          55
Glu Gly Leu Lys Glu Arg Leu Val Leu Val Pro Lys Glu Lys His Asp
                                          75
                      70
Gln Tyr Lys Glu Arg Leu Glu Lys Glu Ile Glu Val Ile Thr Asn Met
 65
                                      90
Lys Phe Pro Gly Tyr Met Leu Ile Val Trp Asp Phe Ile Arg Tyr Ala
                                 105
             100
 Lys Glu Met Gly Ile Pro Val Gly Pro Gly Arg Gly Ser Ala Ala Gly
                                                 125
                             120
 Ser Leu Val Ala Phe Ala Leu Lys Ile Thr Asp Ile Asp Pro Leu Lys
                                             140
                         135
 Tyr Asp Leu Leu Phe
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 <213> Helicobacter pylori
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 <222> (1)..(147)
 <400>.41
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                                                                    48
 Gln Tyr Asp Phe Lys Ala Met Phe Thr Pro Leu Ile Met Gln Ala Gln
                                      10
 ttg agc tta aga aac att gat aat ttt gtg gaa aaa ggc tct gct ttg
 Leu Ser Leu Arg Asn Ile Asp Asn Phe Val Glu Lys Gly Ser Ala Leu
                                  25
 ata gat aaa ttt gac gct aac ccc tat aaa acg att ttt gga gaa agg
 Ile Asp Lys Phe Asp Ala Asn Pro Tyr Lys Thr Ile Phe Gly Glu Arg
                              40
                                                                    147
 aaa
 Lys
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<210> 42
<211> 49
<212> PRT
<213> Helicobacter pylori
<400> 42
Gln Tyr Asp Phe Lys Ala Met Phe Thr Pro Leu Ile Met Gln Ala Gln
                                     10
Leu Ser Leu Arg Asn Ile Asp Asn Phe Val Glu Lys Gly Ser Ala Leu
                                 25
             20
Ile Asp Lys Phe Asp Ala Asn Pro Tyr Lys Thr Ile Phe Gly Glu Arg
                             40
         35
Lys
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<212> DNA
<213> Helicobacter pylori
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<221> CDS
<222> (1)..(453)
<400> 43
aat ttc aat tca gcg aat att act acg agt ttg aat aat tcc tct atc
                                                                   48
Asn Phe Asn Ser Ala Asn Ile Thr Thr Ser Leu Asn Asn Ser Ser Ile
                                     10
                 -5
gtg ttt aag ggg gcg gtc tct tta gga ggg cag ttt aat tta agc aat
Val Phe Lys Gly Ala Val Ser Leu Gly Gly Gln Phe Asn Leu Ser Asn
                                 25
            20
aac tot tot tta gat tto caa ggo tot ago got ato acc tot aac acg
Asn Ser Ser Leu Asp Phe Gln Gly Ser Ser Ala Ile Thr Ser Asn Thr
                                                 45
                             40
gcg ttt aat ttc tat gat aac gct ttt tct caa agc ccc atc act ttc
Ala Phe Asn Phe Tyr Asp Asn Ala Phe Ser Gln Ser Pro Ile Thr Phe
                         55
cat caa gcc ctt gac att aaa gcg ccc tta agt ttg gga ggc aac ctt
                                                                   240
His Gln Ala Leu Asp Ile Lys Ala Pro Leu Ser Leu Gly Gly Asn Leu
                                         75
tta aac cct aac aac age agc gtg ctg gat tta aaa aac agc cag ctt
                                                                   288
Leu Asn Pro Asn Asn Ser Ser Val Leu Asp Leu Lys Asn Ser Gln Leu
                                     90
gtt ttt ggc gat caa ggg agt ttg aat atc gct aac att gat tta cta
                                                                   336
Val Phe Gly Asp Gln Gly Ser Leu Asn Ile Ala Asn Ile Asp Leu Leu
                                105
            100
ago gat ota aat gat aat aaa aat ogt gtg tat aac atc att caa gog
Ser Asp Leu Asn Asp Asn Lys Asn Arg Val Tyr Asn Ile Ile Gln Ala
                            120
gac atg aat agt aat tgg tat gag cgt atc agc ttc ttt ggc atg cac
                                                                   432
Asp Met Asn Ser Asn Trp Tyr Glu Arg Ile Ser Phe Phe Gly Met His
                        135
    130
                                                                   455
atc aat gac ggg att tat gat gc
Ile Asn Asp Gly Ile Tyr Asp
145
<210> 44
<211> 151
<212> PRT
<213> Helicobacter pylori
<400> 44
Asn Phe Asn Ser Ala Asn Ile Thr Thr Ser Leu Asn Asn Ser Ser Ile
                                     10
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Val Phe Lys Gly Ala Val Ser Leu Gly Gly Gln Phe Asn Leu Ser Asn
Asn Ser Ser Leu Asp Phe Gln Gly Ser Ser Ala Ile Thr Ser Asn Thr
```

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40
Ala Phe Asn Phe Tyr Asp Asn Ala Phe Ser Gln Ser Pro Ile Thr Phe
                         55
His Gln Ala Leu Asp Ile Lys Ala Pro Leu Ser Leu Gly Gly Asn Leu
                                         75
Leu Asn Pro Asn Asn Ser Ser Val Leu Asp Leu Lys Asn Ser Gln Leu
                                     90
                 85
Val Phe Gly Asp Gln Gly Ser Leu Asn Ile Ala Asn Ile Asp Leu Leu
                                105
            100
Ser Asp Leu Asn Asp Asn Lys Asn Arg Val Tyr Asn Ile Ile Gln Ala
                                                125
                            120
Asp Met Asn Ser Asn Trp Tyr Glu Arg Ile Ser Phe Phe Gly Met His
                        135
Ile Asn Asp Gly Ile Tyr Asp
                    150
145
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<213> Helicobacter pylori
<220>
<221> CDS
<222> (1)..(333)
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                                                                   48
Asp Phe Ser Phe Asn Ala Gln Gly Asn Val Phe Val Gln Asn Ser Thr
                                     10
                  5
tto tot aac goo aat gga ggo acg oto tot tit aac goa gga aat tog
                                                                   96
Phe Ser Asn Ala Asn Gly Gly Thr Leu Ser Phe Asn Ala Gly Asn Ser
                                 25
             20
ctc att ttt gcc gga aac aat cat att gca ttc act aac cac gct gga
                                                                   144
Leu Ile Phe Ala Gly Asn Asn His Ile Ala Phe Thr Asn His Ala Gly
                             40
act ctt caa tta ttg tcc gat caa gtt tct aac att aac atc acc acg
                                                                   192
Thr Leu Gln Leu Leu Ser Asp Gln Val Ser Asn Ile Asn Ile Thr Thr
                                             60
                         55
ctt aac gct agc aac ggc ctt aag att aac gcc gct aat aac aat gtt
                                                                   240
Leu Asn Ala Ser Asn Gly Leu Lys Ile Asn Ala Ala Asn Asn Asn Val
                                         75
                     70
 65
tot gtg tot caa ggc aat ctg ttt gtc agc gct agc tgc gcg caa caa
                                                                   288
Ser Val Ser Gln Gly Asn Leu Phe Val Ser Ala Ser Cys Ala Gln Gln
                                     90
                 85
age gat cea act aca get aat att gea aac eet tge geg ett age
                                                                   333
Ser Asp Pro Thr Thr Ala Asn Ile Ala Asn Pro Cys Ala Leu Ser
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<211> 111
<212> PRT
<213> Helicobacter pylori
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Asp Phe Ser Phe Asn Ala Gln Gly Asn Val Phe Val Gln Asn Ser Thr
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Phe Ser Asn Ala Asn Gly Gly Thr Leu Ser Phe Asn Ala Gly Asn Ser
                                 25
Leu Ile Phe Ala Gly Asn Asn His Ile Ala Phe Thr Asn His Ala Gly
Thr Leu Gln Leu Leu Ser Asp Gln Val Ser Asn Ile Asn Ile Thr Thr
Leu Asn Ala Ser Asn Gly Leu Lys Ile Asn Ala Ala Asn Asn Asn Val
                     70
                                         75
Ser Val Ser Gln Gly Asn Leu Phe Val Ser Ala Ser Cys Ala Gln Gln
                                     90
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Ser Asp Pro Thr Thr Ala Asn Ile Ala Asn Pro Cys Ala Leu Ser
                                105
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<211> 674
<212> DNA
<213> Helicobacter pylori
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<221> CDS
<222> (1)..(672)
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Leu Arg Leu Gly Gln Phe Asn Gly Asn Ser Phe Thr Ser Tyr Lys Asp
                                     10
                  5
age get gat ege ace acg aga gtg gat tte aac get aaa aat ate tta
                                                                   96
Ser Ala Asp Arg Thr Thr Arg Val Asp Phe Asn Ala Lys Asn Ile Leu
             20
att gat aat ttt tta gaa atc aat aat cgt gtg ggt tct gga gcc ggg
Ile Asp Asn Phe Leu Glu Ile Asn Asn Arg Val Gly Ser Gly Ala Gly
         35
agg aaa gcc agc tct acg gtt tta act ttg caa gct tca gaa ggg att
                                                                   192
Arg Lys Ala Ser Ser Thr Val Leu Thr Leu Gln Ala Ser Glu Gly Ile
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act age agt aaa aat geg gaa att tet ett tat gat gge gee aeg ete
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Thr Ser Ser Lys Asn Ala Glu Ile Ser Leu Tyr Asp Gly Ala Thr Leu
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aat ttg gct tca aac agc gtt aaa tta atg ggt aat gtg tgg atg ggc
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Asn Leu Ala Ser Asn Ser Val Lys Leu Met Gly Asn Val Trp Met Gly
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cqt ttg caa tat gtg gga gcg tat ttg gcc cct tca tac agc acg ata
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Arg Leu Gln Tyr Val Gly Ala Tyr Leu Ala Pro Ser Tyr Ser Thr Ile
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            100
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aac act tca aaa gtg aca ggg gaa gtg aat ttt aac cat ctc act gtg
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Asn Thr Ser Lys Val Thr Gly Glu Val Asn Phe Asn His Leu Thr Val
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                                                125
        115
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ggc gat cac aac gcc gct caa gca ggc att atc gct agt aac aag act
Gly Asp His Asn Ala Ala Gln Ala Gly Ile Ile Ala Ser Asn Lys Thr
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                        135
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His Ile Gly Thr Leu Asp Leu Trp Gln Ser Ala Gly Leu Asn Ile Ile
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                                        155
gcc cct cca gaa ggc ggt tat aag gat aaa cct aag gat aaa cct agt
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Ala Pro Pro Glu Gly Gly Tyr Lys Asp Lys Pro Lys Asp Lys Pro Ser
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Asn Thr Thr Gln Asn Asn Ala Asn Asn Asn Gln Gln Asn Ser Ala Gln
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            180
aac aat agt aac act cag gtt att aac cca ccc aat agc gcg caa aaa
Asn Asn Ser Asn Thr Gln Val Ile Asn Pro Pro Asn Ser Ala Gln Lys
                            200
                                                205
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aca gaa att caa ccc acg caa gtc att gat ggg cct ttt gct ggt ggc
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Arg Lys Ala Ser Ser Thr Val Leu Thr Leu Gln Ala Ser Glu Gly Ile
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Thr Ser Ser Lys Asn Ala Glu Ile Ser Leu Tyr Asp Gly Ala Thr Leu
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Asn Leu Ala Ser Asn Ser Val Lys Leu Met Gly Asn Val Trp Met Gly
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Arg Leu Gln Tyr Val Gly Ala Tyr Leu Ala Pro Ser Tyr Ser Thr Ile
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Asn Thr Ser Lys Val Thr Gly Glu Val Asn Phe Asn His Leu Thr Val
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                            120
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Gly Asp His Asn Ala Ala Gln Ala Gly Ile Ile Ala Ser Asn Lys Thr
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                        135
His Ile Gly Thr Leu Asp Leu Trp Gln Ser Ala Gly Leu Asn Ile Ile
                                        155
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Ala Pro Pro Glu Gly Gly Tyr Lys Asp Lys Pro Lys Asp Lys Pro Ser
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                                    170
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Asn Thr Thr Gln Asn Asn Ala Asn Asn Asn Gln Gln Asn Ser Ala Gln
                                185
            180
Asn Asn Ser Asn Thr Gln Val Ile Asn Pro Pro Asn Ser Ala Gln Lys
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              - 5
  1
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Asn Gly Tyr Val Phe Val Asn Asn Ser Ser Phe Ser Asn Ala Thr Gly
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                                 25
 ggc agt ttg aat ttt gtc gcc aac aag tct att att ttt aat ggc gat
Gly Ser Leu Asn Phe Val Ala Asn Lys Ser Ile Ile Phe Asn Gly Asp
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                              40
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Asn Thr Ile Asp Phe Ser Lys Tyr Gln Gly Ala Leu Ile Phe Ala Ser
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                          55
 aat gat gtt tct aat atc aat atc acc acc cta aac gct act aat ggc
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 Asn Asp Val Ser Asn Ile Asn Ile Thr Thr Leu Asn Ala Thr Asn Gly
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 tta agc ctt aat gcg ggt ttg aat aac gtg agc gtt caa aaa gg
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 Gly Ser Leu Asn Phe Val Ala Asn Lys Ser Ile Ile Phe Asn Gly Asp
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Asn Thr Ile Asp Phe Ser Lys Tyr Gln Gly Ala Leu Ile Phe Ala Ser
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gac cca agg ctt tat ggt atg gta acc tta gac caa atc cat gaa atc
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Asp Pro Arg Leu Tyr Gly Met Val Thr Leu Asp Gln Ile His Glu Ile
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atg caa act ttc gtg aaa caa ggc aat tta gat gtg gaa tta gag ttt
Met Gln Thr Phe Val Lys Gln Gly Asn Leu Asp Val Glu Leu Glu Phe
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ttt caa act aat ttt gag ggc gaa atc att gat aaa atc caa gag agc
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Phe Gln Thr Asn Phe Glu Gly Glu Ile Ile Asp Lys Ile Gln Glu Ser
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                                              60
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Val Gly Ser Asp Tyr Glu Gly Ile Ile Ile Asn Pro Gly Ala Phe Ser
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cac act tot att gog att goa gat gog atc atg ota gog ggc aaa coc
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His Thr Ser Ile Ala Ile Ala Asp Ala Ile Met Leu Ala Gly Lys Pro
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                                     90
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Gly Pro Leu Gly Tyr Asn Met Ala Leu Met Ala Met Val Asn Ile Leu
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Met Gln Thr Phe Val Lys Gln Gly Asn Leu Asp Val Glu Leu Glu Phe
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Phe Gln Thr Asn Phe Glu Gly Glu Ile Ile Asp Lys Ile Gln Glu Ser
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His Thr Ser Ile Ala Ile Ala Asp Ala Ile Met Leu Ala Gly Lys Pro
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Val Ile Glu Val His Leu Thr Asn Ile Gln Ala Arg Glu Glu Phe Arg
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Lys Asn Ser Tyr Thr Gly Ala Ala Cys Gly Gly Val Ile Met Gly Phe
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                            120
Gly Pro Leu Gly Tyr Asn Met Ala Leu Met Ala Met Val Asn Ile Leu
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  Asn Phe Asn Asn Thr Gly Ser Val Asn Ile Ser Gly Asn Ala Thr Phe
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  gat aat gtg gtg ttt aat ggc cct acg aac acg agc gtg aaa ggg cag
  Asp Asn Val Val Phe Asn Gly Pro Thr Asn Thr Ser Val Lys Gly Gln
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  gtt act tta aat aac atc act tta aaa aac ctg aac gcc cet ttg tct
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	Thr			85					90					95		
+++	ggc	ast	~~~	200	att	act	ttt	aac	act	cat	tca	ata	att	aat	att	336
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act	gaa	tct	atc	act	aat	aac	aac	cct	atc	act	ctt	qta	agc	tct	tct	384
get	Glu	0	71-	mb-	3	61	Acn	Dro	Tla	Thr	T.em	۷эl	Ser	Ser	Ser	
ATa	GIU		116	Inr	ASII	GTA		110	116	1111	LCu	105				
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-	Glu	T1-	900	m	2	7	717	Dha	Sor	Lue	Aen	T.e.n	Trn	Gln	T.e.11	
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71-	Asn	m	C1-	C1	ui.	Glv	۸la	Ser	Ser	Ğlıı	T.vs	Leu	Val	Ser	Ser	
	ASII	TYL	GIII	Gry		0+3				155	-1-				160	
145					150											500
qcq	ggt	aat	ggc	gtt	tat	gat	gtg	gtg	tat	tct	ttc	aat	aac	caa	acc	528
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ALG	GLY			165	-1-				170					175		
			*												~~+	576
tac	aat	ttc	caa	gag	gtt	ttt	tca	caa	aac	agc	att	ECL	acc	cgg	cgt	370
Tvr	Asn	Phe	Gln	Glu	Val	Phe	Ser	Gln	Asn	Ser	Ile	Ser	Ile	Arg	Arg	
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	ggc			-+-	-t-	+++	ast		ata	na t	ato	m2 2		tca	gat	624
ttg	ggc	gtt	aac	acg	grā		yac	- Lar	grg	gac	acg	900	T	Con	3	٠
Leu	Gly	Val	Asn	Met	Val	Phe	Asp	Tyr	Val	Asp	met	GIU	гÀг	ser	Asp	
	_	195					200					205				
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Cat	LLd	Lat	-	Caa	100	31-	1	63	Dha	Mat	The	Tur	Mot	Dro	Aen	
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His Leu Asn Phe Asn Gly Ala Val Asn Phe Asn Ser Ala Asn Ile Thr
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acg agt ttg aat aat tcc tct atc gtg ttt aag ggg gcg gtc tct tta
Thr Ser Leu Asn Asn Ser Ser Ile Val Phe Lys Gly Ala Val Ser Leu
                             40
gga ggg cag ttt aat tta agc aat aac tct tct tta gat ttc caa ggc
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Gly Gly Gln Phe Asn Leu Ser Asn Asn Ser Ser Leu Asp Phe Gln Gly
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Ser Ser Ala Ile Thr Ser Asn Thr Ala Phe Asn Phe Tyr Asp Asn Ala
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                     70
ttt tet caa age eec ate act tte cat caa gee ett gae att aaa geg
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Phe Ser Gln Ser Pro Ile Thr Phe His Gln Ala Leu Asp Ile Lys Ala
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                 85
ccc tta agt ttg gga ggc aac ctt tta aac cct aac agc agc gtg
                                                                   336
Pro Leu Ser Leu Gly Gly Asn Leu Leu Asn Pro Asn Asn Ser Ser Val
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            100
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Leu Asp Leu Lys Asn Ser Gln Leu Val Phe Gly Asp Gln Gly Ser Leu
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                             120
aat atc gct aac att gat tta cta agc gat cta aat gat aat aaa aat
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Asn Ile Ala Asn Ile Asp Leu Leu Ser Asp Leu Asn Asp Asn Lys Asn
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cgt gtg tat aac atc att caa gcg gac atg aat agt aat tgg tat gag
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Arg Val Tyr Asn Ile Ile Gln Ala Asp Met Asn Ser Asn Trp Tyr Glu
                                         155
 cgt atc agc ttc ttt ggc atg cac atc aat gac ggg att tat gat gct
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 Arg Ile Ser Phe Phe Gly Met His Ile Asn Asp Gly Ile Tyr Asp Ala
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 aaa aac caa act tat agt ttc act aac ccc ctt aat aac gcc cta aaa
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 Lys Asn Gln Thr Tyr Ser Phe Thr Asn Pro Leu Asn Asn Ala Leu Lys
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 atc acc gag agc ttt aaa gac aac caa cta agc gtt acg ctc tct caa
                                                                    624
 Ile Thr Glu Ser Phe Lys Asp Asn Gln Leu Ser Val Thr Leu Ser Gln
                                                 205
                             200
         195
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                                                                    672
 Ile Pro Gly Ile Lys Asn Thr Leu Tyr Asn Ile Gly Ser Glu Ile Phe
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                         215
 aac tac caa aaa gtt tat aac aac gct aat ggc gtg tat tct tat agc
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Thr Ser Leu Asn Asn Ser Ser Ile Val Phe Lys Gly Ala Val Ser Leu
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Gly Gly Gln Phe Asn Leu Ser Asn Asn Ser Ser Leu Asp Phe Gln Gly
Ser Ser Ala Ile Thr Ser Asn Thr Ala Phe Asn Phe Tyr Asp Asn Ala
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Phe Ser Gln Ser Pro Ile Thr Phe His Gln Ala Leu Asp Ile Lys Ala
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Pro Leu Ser Leu Gly Gly Asn Leu Leu Asn Pro Asn Asn Ser Ser Val
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Leu Asp Leu Lys Asn Ser Gln Leu Val Phe Gly Asp Gln Gly Ser Leu
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        115
                            120
Asn Ile Ala Asn Ile Asp Leu Leu Ser Asp Leu Asn Asp Asn Lys Asn
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Arg Val Tyr Asn Ile Ile Gln Ala Asp Met Asn Ser Asn Trp Tyr Glu
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Arg Ile Ser Phe Phe Gly Met His Ile Asn Asp Gly Ile Tyr Asp Ala
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Lys Asn Gln Thr Tyr Ser Phe Thr Asn Pro Leu Asn Asn Ala Leu Lys
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Ile Thr Glu Ser Phe Lys Asp Asn Gln Leu Ser Val Thr Leu Ser Gln
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Ile Pro Gly Ile Lys Asn Thr Leu Tyr Asn Ile Gly Ser Glu Ile Phe
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                                     10
tta agg gct aaa aat atc cat atc aat ttc caa ggc gtt tct act ttt
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Leu Arg Ala Lys Asn Ile His Ile Asn Phe Gln Gly Val Ser Thr Phe
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             20
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Lys Gln Asn Ser Thr Met Asn Leu Ala Glu Ser Ser Gln Ala Ser Phe
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                             40
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Asn Ala Leu Lys Val Glu Gly Glu Thr Asn Phe Asn Leu Asn Asn Ser
                         55
                                             60
age ttg ttg aat tte aat gge aat age gtt tte aae get eet gtg agt
Ser Leu Leu Asn Phe Asn Gly Asn Ser Val Phe Asn Ala Pro Val Ser
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Phe Tyr Ala Asn His Ser Gln Ile Ser Phe Thr Lys Leu Ala Thr Phe
                 85
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Gln	Ser	_	Leu	Leu	Asn	GIA	ATA	Leu	ASn	rea	Leu	125	POII	Gry	Der	•
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aac	aat Asn	cta	gcg	atc	aac	Ala	Luc	61 v	Asn	Phe	Ser	Phe	Glv	Ser	Lvs	
Asn		Leu	ATA	TTE	ASII	135	פעם	U .,			140		2			
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1 45					150					155					100	
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Thr	Ser	Val	Tyr	Asp	Val	Leu	Gln	Ala	Gln	Asn	Ile	Asp	Gly	ren	Met	
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Gly	Asn	Asn		Tyr	Glu	Lys	Ile	Arg	Phe	Tyr	GTĀ	116	190	TIE	Asp	
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aag	gct Ala	gat	tac	tcg	ttt	gat	aac	ggc	yet Val	Hie	Ser	Tro	Ara	Phe	Thr	024
Lys	Ala		Tyr	Ser	Pne	Asp	200	GIY	vaı	птэ	562	205	9			•
	ccg	195	+	200	act	na a		att	aca	σаа	acc		cat	aac	aac	672
aac	CCG	Tou	Acn	Thr	Thr	Glu	Thr	Ile	Thr	Glu	Thr	Leu	His	Asn	Asn	
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Ara	Leu	Lvs	Val	Gln	Ile	Ser	Gln	Asn	Gly	Val	Ser	Asn	Asn	Lys	Met	•
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Phe	Asn	Leu	Ala	Pro	Ser	Leu	Tyr	Asp	Tyr	Gln	Lys	Asn	PIO	IğI	Asn	
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gaa	acc	gag	aat	tcc	tat	aat	tac	aca	agc	gat	aag	yr.	Glu	Thr	tat	010
Glu	Thr	Glu		Ser	Tyr	Asn	туг	265	Ser	nsp	пуз	VOL	270		Tyr	
			260	+	ato	222	aac		aat	caa	aac	aat		aca	CCC	864
tat	tta	acg	agc Sor	Acr	Tle	Lve	Glv	Phe	Asn	Gln	Asn	Asn	Lys	Thr	Pro	
Tyr	Leu	275	Ser	ASII	116	2,5	280					285	-	•		
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999 G1v	Thr	Tvr	Asn	Ala	Gln	Asn	Gln	Pro	Leu	Gln	Ala	Leu	His	Ile	Tyr	
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aat	036	gct	atc	act	aag	caa	gat	ttg	aac	atg	atc	gcc	agt	ttg	ggt	960
Asn	Gln	Ala	Ile	Thr	Lys	Gln	Asp	Leu	Asn	Met	Ile	Ala	Ser	Leu	GTA	
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aag	gag	ttt	ttg	cct	aaa	ata	gcc	aat	ct							989
Lys	Glu	Phe	Leu			Ile	Ala	Asn								
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Lvs	Gln	Asn	Ser	Thr	Met	Asn	Leu	Ala	Glu	Ser	Ser	Gln	Ala	Ser	Phe	
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Phe	Tyr	Ala	Asn	His	Ser	Gln	Ile	Ser	Phe	rnr	гÀг	ren	WT9	inr	Phe	

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Thr				165	Val				170	•				Leu 175		
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Phe			_	245					250					Tyr 255		
			260					265					270	Thr		
_		275					280					285		Thr		
_	290					295					300			Ile		
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Lys	Glu	Phe	Leu	Pro 325	Lys	Ile	Ala	Asn								
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1 ttt	++=	acσ	cat	gcc	аσа	aaa	aac	ttg	cct	ttc	acg	gct	aaa	att	gaa	96
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att	gcc	gct	tat	aga	gat	gcg	cat	Tur	Pro	Phe	gcc Val	T.e.n	Len	Glu	gcg Ala	210
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ago	999	aac	att	tca	cta	gag	agc	מננ סוד	Agn	Ala	Tvr	Ala	Lvs	Ser	ggc Gly	200
	_			85					90					95		336
gtg	gat	gcc	att	agc	gta v=1	9 <b>9</b> 9	yct Ala	Len	Ile	His	Gln	Ala	Thr	Phe	att Ile	
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Ala Asp Ile Val Met Cys Asp Asn Leu Ser Val Leu Glu Thr Lys Glu
                         55
                                              60
Ile Ala Ala Tyr Arg Asp Ala His Tyr Pro Phe Val Leu Leu Glu Ala
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Ser Gly Asn Ile Ser Leu Glu Ser Ile Asn Ala Tyr Ala Lys Ser Gly
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Val Asp Ala Ile Ser Val Gly Ala Leu Ile His Gln Ala Thr Phe Ile
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gtg gat ttg gaa tgg ttt gaa acg agg aaa aaa atc gct cgt ttt aaa
Val Asp Leu Glu Trp Phe Glu Thr Arg Lys Lys Ile Ala Arg Phe Lys
                                  25
             20
ace agg caa ggc aaa gac ata gcc ata cgc ctt aaa gac gct ccc aag
                                                                    144
Thr Arg Gln Gly Lys Asp Ile Ala Ile Arg Leu Lys Asp Ala Pro Lys
                              40
ttg ggg ctc tct caa ggg gat att tta ttt aaa gaa gag aag gaa att
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Leu Gly Leu Ser Gln Gly Asp Ile Leu Phe Lys Glu Glu Lys Glu Ile
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atc gcc gtt aat atc ttg gat tct gaa gtc att cac atc caa gcc aag
                                                                    240.
Ile Ala Val Asn Ile Leu Asp Ser Glu Val Ile His Ile Gln Ala Lys
                                          75
age gtg gca gaa gta gcg aaa ata tgc tat gaa ata gga aac cgc cat
                                                                    288
Ser Val Ala Glu Val Ala Lys Ile Cys Tyr Glu Ile Gly Asn Arg His
                  85
gcg gct tta tac tat ggc gag tct caa ttt gaa ttt aaa aca cca ttt
                                                                    336
Ala Ala Leu Tyr Tyr Gly Glu Ser Gln Phe Glu Phe Lys Thr Pro Phe
                                 105
gaa aag ccc acg cta gcg tta tta gaa aag cta ggg gtt caa aat cgt
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Glu Lys Pro Thr Leu Ala Leu Leu Glu Lys Leu Gly Val Gln Asn Arg
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                             120
         115
 gtt tta agt tca aaa ttg gat tcc aaa gaa cgc tta acc gtg agc atg
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Leu Gly Leu Ser Gln Gly Asp Ile Leu Phe Lys Glu Glu Lys Glu Ile
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Ser Val Ala Glu Val Ala Lys Ile Cys Tyr Glu Ile Gly Asn Arg His
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Ala Ala Leu Tyr Tyr Gly Glu Ser Gln Phe Glu Phe Lys Thr Pro Phe
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Lys Thr Ser Asn Ile Glu Thr Asn Asn Gln Ile Lys Val Glu Gln Glu
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aaa caa aag aca agc aat ata gag act aat aat caa ata aaa gta gaa
Lys Gln Lys Thr Ser Asn Ile Glu Thr Asn Asn Gln Ile Lys Val Glu
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caa gaa caa caa aag aca agc aat aca cag aaa gat ttg gtt aaa gaa
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Gln Glu Gln Gln Lys Thr Ser Asn Thr Gln Lys Asp Leu Val Lys Glu
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cag aaa gat ttg gtt aaa gaa cag aaa gat ttg gtt aaa gaa cag aaa
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Gln Lys Asp Leu Val Lys Glu Gln Lys Asp Leu Val Lys Glu Gln Lys
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gat ttg gtt aaa gaa cag aaa gat ttg gtt aaa aca cag aaa gat ttc
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Asp Leu Val Lys Glu Gln Lys Asp Leu Val Lys Thr Gln Lys Asp Phe
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att aaa tat gta gaa caa aat tgc caa gaa aat cat aat caa ttc ttt
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Ile Lys Tyr Val Glu Gln Asn Cys Gln Glu Asn His Asn Gln Phe Phe
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                                105
            100
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Ile Glu Lys Gly Gly Ile Lys Ala Gly Ile Gly Ile Glu Val Glu Ala
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gaa tgc aaa acc cct aaa cct gca aaa acc aat caa acc cct atc cag
Glu Cys Lys Thr Pro Lys Pro Ala Lys Thr Asn Gln Thr Pro Ile Gln
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  130
 cca aaa cac ctc cca aac tct aaa caa ccc cgc tct caa aga gga tca
Pro Lys His Leu Pro Asn Ser Lys Gln Pro Arg Ser Gln Arg Gly Ser
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Lys	gcg Ala	Gln	Glu	Leu	Ile	Ála	Tyr	Leu	GIII	Lys	Glu	Leu	Glu	Phe 175	Leu	
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CCC	tat Tyr	Ser	Gln	Lvs	Ala	Ile	Ala	Lys	Gln	Val	Asp	Phe	Tyr	Arg	Pro	
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Ğlu	Glu	Trp	Gln	Lys	Glu	Asn 215	Leu	Lys	He	Arg	220	гÀ2	ATG	GIII	VIG	
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Lys	atg Met	Leu	Glu	Met	Arg	Asn	Pro	Gln	Ala	піз	Leu	Ser	Asn	Ser	Gln 240	
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									TO							
	Thr		าก					2.3							Glu	
_		25	Thr	Ser			40					4.5	,		Glu	
		Gln	Gln			יי יי					UU				Glu	•
	Lys	Asp			70					13					Lys 80	
Asp	Leu			OE					90					~~		
			707	Glu	Gln			103							Phe	•
Ιle	e Glu	Lys	Gly	Gly	Ile	Lys	Ala	Gly	Ile	Gly	Ile	Glu 125	ı Val	Glu	Ala	
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Pro	Lys	: His	Leu	Pro	Asn	Ser	Lys	Gln	Pro	Arg 155	j Ser	GII	Arc	i erz	Ser 160	
145	5		. 61.	. I.a.ı	150 Tle	l Ala	Tvr	Leu	Glr	Lys	, Glu	Let	ı Glu	ı Phe	Leu	
				165					1/1	,					,	
			1 0 /	`				TRE	)				15	,	Pro	
		101	=				- 200	)	•			20.	,		l Thr	
	01/	`				715	)				22	,			Ala	
	s Met	t Le	ı Glı	ı Met	Arg	y Asr	Pro	Glr	n Ala	His 235	E Leu	ı Sei	r Ası	ı Sei	Gln 240	
22	5 ~ T ^:	ים. ז	ı Ph	a Val	230 L Glr	, Lvs	: Ile	e Phe	a Ala	Asp	Val	l Ası	n Ly:	s Glu	Ile	
Se:	T De	וטע א		245	5				250	) ·				25	5	

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Ser Gly Glu Tyr Cys Val Ser Thr Asp Ser Phe Val Ile Thr Pro Leu
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Phe Ile Leu Glu Glu Gly Leu Glu Ile Ser Leu Leu Lys Gln Ile Leu
caa tcc ata caa aaa gaa ttg ttt aaa gcc aac ctg aaa ctc ctc tcc
                                                                   288
Gln Ser Ile Gln Lys Glu Leu Phe Lys Ala Asn Leu Lys Leu Leu Ser
cta gac act aaa gtc gtg cca aag ggg agc gtg gat aag ctt ttt atc
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Leu Asp Thr Lys Val Val Pro Lys Gly Ser Val Asp Lys Leu Phe Ile
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aac aca acc tgc att ggt aaa atc atc aag cca ggg att tct tcg tac
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Asn Thr Thr Cys Ile Gly Lys Ile Ile Lys Pro Gly Ile Ser Ser Tyr
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                            120
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Asn Leu Glu Ser Asp Cys Gln Leu Leu Tyr Pro Leu Leu Lys Pro Leu
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                165
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Phe Leu Ser Asp Leu Lys Ile Asp Ala Leu Arg Asp Ala Thr Arg Gly
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ggg tta gcg agc gtg ctg aac gaa tgg gcg aac agc tct aga gtg aaa
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Gly Leu Ala Ser Val Leu Asn Glu Trp Ala Asn Ser Ser Arg Val Lys
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        195
atc gtt ata gaa gaa gaa aaa atc ccc tta aaa gaa gaa acg aaa ggg
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Ile Val Ile Glu Glu Glu Lys Ile Pro Leu Lys Glu Glu Thr Lys Gly
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                        215
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                                        235
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                                                                   768
Val Phe Val Leu Ala Leu Asn Gln Lys Asp Ala Pro Lys Ala Leu Glu
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                245
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Cys
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Gln Ser Ile Gln Lys Glu Leu Phe Lys Ala Asn Leu Lys Leu Leu Ser
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Leu Asp Thr Lys Val Val Pro Lys Gly Ser Val Asp Lys Leu Phe Ile
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Asn Leu Glu Ser Asp Cys Gln Leu Leu Tyr Pro Leu Leu Lys Pro Leu
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Phe Leu Ser Asp Leu Lys Ile Asp Ala Leu Arg Asp Ala Thr Arg Gly
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                            200
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Arg	Phe	Lys	Asn 100	Asp	Asp	Ala	Leu	Leu 105	Glu	Cys	Ala	гÄг	110	116	GIÜ	
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gcc Ala	aaa Lys	cag Gln	cat His	gcg Ala 165	ttt Phe	ttg Leu	aac Asn	gcg Ala	Leu 170	gaa Glu	Cys	Glu	Ser	Leu 175	Ile	
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Pro	Tyr	Thr	Pro	Leu	His	Ala 215	Leu	Leu	Leu	Asp	Leu 220	Leu	Asp	Pne	Pro	
Ile	gtg Val	ttc	acg Thr	agc Ser	Ala	aat Asn	ttc Phe	agc Ser	tcc Ser	Leu	cct Pro	tta Leu	gcg Ala	agc Ser	gat Asp 240	720
gag	act	gag	att	gac	230 gcc Ala	ttg Leu	agt Ser	ttc Phe	att Ile	235 ttt Phe	gat Asp	ttt Phe	aag Lys	ctc Leu	acg	768
	220	cac	act	245 atc	atc	cat	agg	att	250 gat	gac	agc	atc	gtg	cag	cat	816
His	Asn	Arg	Ala 260	Ile	Ile	His	Arg	11e 265	Asp	Asp	Ser	ITE	270	GIN	HIS	064
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ctt Lev	tac Tyr	ctc	acc	ttg Leu	cct Pro	aaa Lys	cgc Arg	tct Ser	aat Asn	ggt Gly	Ser	Pro	aaa Lys	aag Lys	att Ile	912
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gga	Thr	250	71-	Tan	ton	Tan	Cor	Dro	Dhe	Cvs	Glv	Asp	Leu	Ser	Val	
GTA	Tnr	Ser	iie		ьeu	Leu	261	110	330	Cys	01,	· · · · ·		335		
				325						++~	22+	+++	ttc		222	1056
tta	gaa	aat	gaa	aaa	cac	ttt	aaa	gaa	act	ttg	aat	בננ	Dha	Tan	aaa 7	1030
Leu	Glu	Asn	Glu	Lys	His	Phe	Lys		Thr	Leu	Asn	Pne	rne	Leu	ràs	
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Thr	Tyr	Asp	Phe	Ĺуs	Pro	Thr	Ile	Leu	Ala	Cys	Asp	Lys	His	Gln	Asn	
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Tur	Thr	Thr	Thr	Gln	Met	Ala	Phe	Asp	Phe	Asn	Thr	Pro	Leu	Leu	Gln	
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	GIII	птэ	ura	1113	390			200		395					400	
385	caa					+	~~~	000	+++		aac	att	atc	taa		1248
tta	caa	gat	ccg	Cat	LLa	aat Nam	uic	Dec	Dha	Tla	610	Tla	Val	Trn	Aen	
Leu	Gln	Asp	Pro		Ļeu	Asn	HIS	PIO		TTE	GIA	116	AGT	415	rop	
				405					410							1206
ggg	agt	ggg	gct	tat	gaa	aat	aag	att	tat	ggg	gcg	gag	tgt	בננ	geg	1296
Gly	Ser	Gly	Ala	Tyr	Glu	Asn	Lys		Tyr	GTA	Ala	GIU	Cys	rne	var	
			420					425					430			
ggg	gat	ttg	gaa	cgc	att	gaa	gaa	acc	gcc	agg	ttt	gaa	gaa	ttt	tgg	1344
Gly	Asp	Leu	Glu	Arg	Ile	Glu	Glu	Thr	Ala	Arg	Phe	Glu	Glu	Phe	Trp	
_		435					440					445				
ctt	tta	aga	ppp	caa	aaa	gcg	atc	aaa	gag	cct	aga	cgc	ctg	gtt	tta	1392
Leu	Leu	ĞÎV	Glv	Gln	Lys	Ala	Ile	Lys	Glu	Pro	Arg	Arg	Leu	Val	Leu	
	450	1	,		-	455		-			460					
gaa	atc	act	tta	aaa	cac	caa	ctc	aac	aag	ctt	tta	aag	cgc	gtt	caa	1440
Glu	Ile	Δla	Len	Lvs	His	Gln	Leu	Asn	Lvs	Leu	Leu	Lys	Arg	Val	Gln	
465	116	nια	DCu		470				3	475		•	-		480	
403	cat	+++	222	722		gaa	tta	gaa	att	ttc	caa	caa	atq	cat	gac	1488
aay	His	Dha	Tue	Clu	Den	Glu	Len	Glu	Tle	Phe	Gln	Gln	Met	His	Asp	
гÀг	птэ	rne	гуз	485	nap	GIG	DCu	<b>01</b> 4	490		<b></b>			495		
	aaa						200	22+		ata	aaa	cat	tta		gat	1536
aaa	aaa Lys	att	caa	agc	ala Tla	31-	mb-	A cr	505	Tla	614	Ara	1.011	Phe	Δen	
Lys	Lys	TTe		ser	116	ATA	IIII		SET	116	Gry	ALY	510	1110	120P	
			500					505						~~~	<b>663</b>	1584
ata	gta	gcg	ttt	agt	ttg	gat	tta -	aca	gga	acg	acc Tl-	age	Dha	Clu	yca Ni-	1304
Ile	Val	Ala	Phe	Ser	Leu	Asp		Thr	GTÅ	Thr	ire		rne	GIU	ALG	
		515					520					525				
gag	agc	ggg	cag	gtt	tta	gaa	aat	cta	gcc	tta	caa	agc	gat	gag	atc	1632
Glu	Ser	Gly	Gln	Val	Leu	Glu	Asn	Leu	Ala	Leu	Gln	Ser	Asp	Glu	Ile	
	530					535					540					
act	ttt	tac	cct	ttt	gaa	atc	aaa	aac	agc	gtg	gtg	tgt	ttg	aaa	gaa	1680
Δla	Phe	Tvr	Pro	Phe	Ğlu	Ile	Lys	Asn	Ser	Val	Val	Cys	Leu	Lys	Glu	
545		-1-	•		550		-			555					560	
+++	tat	caa	aca	+++	gaa	aaσ	gat	tta	aac	att	tta	gag	cct	gaa	cgc	1728
Pho	Tyr	Gln	Δla	Phe	Glu	Lvs	Asp	Leu	ĞÎv	Val	Leu	Glu	Pro	Glu	Arg	
FILE	ıyı	GIII	MIG	565	014	-,-			570					575	-	
	gct			505				at a		na a	atc	att	acc	-	tta	1776
atc	gct Ala	aag	aaa	בננ	ינננ	aac	com	Tau	yca Val	Clu	Tle	Tlo	Thr	Δla	T.eu	
Ile	Ala	ьуs		Pne	Pne	ASII	Ser		AGT	GIU	116	110	590		200	
			580					585	_+-	<b>.</b>		~~~		~+~	+++	1824
atc	gtg	cct	ttt	aaa	gag	cat	gtg	gtg	grg	tgc	agt	999	ggc	gra	Dha	1024
Ile	Val	Pro	Phe	Lys	Glu	His		Val	Val	Cys	Ser	GTA	GTĀ	val	rne	
		595					600					605				
tac	aac	caa	tta	tta	tgc	gaa	caa	tta	gcc	aaa	cga	ttg	aga	ggg	cta	1872
Cvs	Asn	Gln	Leu	Leu	Cys	Glu	Gln	Leu	Ala	Lys	Arg	Leu	Arg	Gly	Leu	
-,-	610				-	615					620					
аал	agg	cao	tat	ttt	ttc	cac	aaq	cat	ttc	ccc	cct	aat	gac	agc	agt	1920
aay	~77	Gln	Tur	Phe	Phe	His	Lvs	His	Phe	Pro	Pro	Asn	Asp	Ser	Ser	
1,170							- 2 -						-			

505					630					635					640	
625	cct	atc	aat	caa	acc	tta	atg	gcg	tat	ttc	aac	cct	aca	atc	atc	1968
Ile	Pro	Ile	Gly	Gln 645	Ála	Leu	Met	Ala	Tyr 650	Phe	Asn	Pro	Thr	Ile 655	Ile	
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		35					40					45		Asn		
	EΛ					55					60			Leu		
65					70					15				Phe	80	
				85					90						•	
_			100					105					110	Ile	•	
_		115					120					123		Leu		
-	130					135					140			Leu		
145					150					122				Asn	100	
Ala				165					170					Leu 175		
			180					185					190			
		1 0 5					200					205		Ile		
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225					230					235				Ser	240	
				245					250					255		
			260					265					2/0			
		275					280					200			Pro	
	200					295					300				Ile	
205					310					312	<b>)</b>				Ser 320	
Gly	Thr			325					330	l				333		
			340	١				345	)				331	,	Lys	
		355					360	)				303	ł		Asn	
_	270	<b>)</b>				375	, .				380				Gln	
Val 385	Glr	His	His	His	390		Phe	Leu	Ala	Ser 395	· Val	Leu	ASP	Ala	400	

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Leu Gln Asp Pro His Leu Asn His Pro Phe Ile Gly Ile Val Trp Asp
                                    410
                405
Gly Ser Gly Ala Tyr Glu Asn Lys Ile Tyr Gly Ala Glu Cys Phe Val
                                                     430
                                425
            420
Gly Asp Leu Glu Arg Ile Glu Glu Thr Ala Arg Phe Glu Glu Phe Trp
                            440
Leu Leu Gly Gly Gln Lys Ala Ile Lys Glu Pro Arg Arg Leu Val Leu
                        455
Glu Ile Ala Leu Lys His Gln Leu Asn Lys Leu Leu Lys Arg Val Gln
                                         475
                    470
Lys His Phe Lys Glu Asp Glu Leu Glu Ile Phe Gln Gln Met His Asp
                                     490
                485
Lys Lys Ile Gln Ser Ile Ala Thr Asn Ser Ile Gly Arg Leu Phe Asp
                                 505
            500
Ile Val Ala Phe Ser Leu Asp Leu Thr Gly Thr Ile Ser Phe Glu Ala
                             520
        515
Glu Ser Gly Gln Val Leu Glu Asn Leu Ala Leu Gln Ser Asp Glu Ile
                                             540
                         535
Ala Phe Tyr Pro Phe Glu Ile Lys Asn Ser Val Val Cys Leu Lys Glu
    530
                                         555
                    550
545
Phe Tyr Gln Ala Phe Glu Lys Asp Leu Gly Val Leu Glu Pro Glu Arg
                                     570
                565
Ile Ala Lys Lys Phe Phe Asn Ser Leu Val Glu Ile Ile Thr Ala Leu
                                                     590
                                 585
            580
Ile Val Pro Phe Lys Glu His Val Val Cys Ser Gly Gly Val Phe
                                                 605
                             600
Cys Asn Gln Leu Leu Cys Glu Gln Leu Ala Lys Arg Leu Arg Gly Leu
                                             620
                         615
Lys Arg Gln Tyr Phe Phe His Lys His Phe Pro Pro Asn Asp Ser Ser
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                    630
Ile Pro Ile Gly Gln Ala Leu Met Ala Tyr Phe Asn Pro Thr Ile Ile
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 gtt aga aaa ttc tat cgg cat aaa aaa tgg gtg gat gca gat gtg tgg
                                                                    96
 Val Arg Lys Phe Tyr Arg His Lys Lys Trp Val Asp Ala Asp Val Trp
                                  25
 caa atg gaa aaa tta ctg cct gga aat gaa gtc ata gga cct gcg atc
 Gln Met Glu Lys Leu Leu Pro Gly Asn Glu Val Ile Gly Pro Ala Ile
                                                  45
                              40
 gtg gaa toa gat gog acc act tto gtg ata occ aaa ggo ttt gog aca
 Val Glu Ser Asp Ala Thr Thr Phe Val Ile Pro Lys Gly Phe Ala Thr
                          55
 aga cta gac aaa cac cga ttg ttc cac ttg aaa gaa att aaa
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 Arg Leu Asp Lys His Arg Leu Phe His Leu Lys Glu Ile Lys
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Gln Met Glu Lys Leu Leu Pro Gly Asn Glu Val Ile Gly Pro Ala Ile
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Arg Leu Asp Lys His Arg Leu Phe His Leu Lys Glu Ile Lys
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Leu Leu Tyr Ser Glu Ile Ile Val Ala Gly Arg Val Ala Arg Asn Glu
                                     10
ttg ttt aaa ttc aac cgc ttg cac acc aaa atc tct att tta caa gat
Leu Phe Lys Phe Asn Arg Leu His Thr Lys Ile Ser Ile Leu Gln Asp
                                 25
             20
gag aaa ccc atc tat tat gac aac acg att tta gat ccc aaa acc acc
Glu Lys Pro Ile Tyr Tyr Asp Asn Thr Ile Leu Asp Pro Lys Thr Thr
                             40
gac tta aat aac atg tgc atg ttt gat ggc tat acg cat tat ttg aat
                                                                   192
Asp Leu Asn Asn Met Cys Met Phe Asp Gly Tyr Thr His Tyr Leu Asn
                         55
ttg gtg ctt gtc aat tgc ccc ata gag ctc tct ggt gtg cga gaa tgc
                                                                   240
Leu Val Leu Val Asn Cys Pro Ile Glu Leu Ser Gly Val Arg Glu Cys
                     70
att gaa gaa agc gaa ggg gtg gat ggg gca gtg agt gaa acc gct agt
                                                                   288
Ile Glu Glu Ser Glu Gly Val Asp Gly Ala Val Ser Glu Thr Ala Ser
                                     90
tot cat tta tgc gtg aaa gct tta gcg aaa ggc tca gaa ccc tta ttg
                                                                   336
Ser His Leu Cys Val Lys Ala Leu Ala Lys Gly Ser Glu Pro Leu Leu
                                105
            100
cat tta aga gaa aaa atc gct cgc ttg gtt acg caa acc acc acg ca
                                                                   383
His Leu Arg Glu Lys Ile Ala Arg Leu Val Thr Gln Thr Thr
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Leu Phe Lys Phe Asn Arg Leu His Thr Lys Ile Ser Ile Leu Gln Asp
Glu Lys Pro Ile Tyr Tyr Asp Asn Thr Ile Leu Asp Pro Lys Thr Thr
Asp Leu Asn Asn Met Cys Met Phe Asp Gly Tyr Thr His Tyr Leu Asn
Leu Val Leu Val Asn Cys Pro Ile Glu Leu Ser Gly Val Arg Glu Cys
Ile Glu Glu Ser Glu Gly Val Asp Gly Ala Val Ser Glu Thr Ala Ser
Ser His Leu Cys Val Lys Ala Leu Ala Lys Gly Ser Glu Pro Leu Leu
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105
            100
His Leu Arg Glu Lys Ile Ala Arg Leu Val Thr Gln Thr Thr
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Lys Glu Leu Leu Asn Asn His Phe Lys Gln Arg Leu Ala Phe Arg Cys
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aat ggt gag aac ttg agc gct atc aaa aaa gat tta cct cta tta aca
                                                                   96
Asn Gly Glu Asn Leu Ser Ala Ile Lys Lys Asp Leu Pro Leu Leu Thr
                                 25
             20
aac gaa ctc aac gcg cta ttt gta gag ctt tct aaa gac agc cat act
                                                                   144
Asn Glu Leu Asn Ala Leu Phe Val Glu Leu Ser Lys Asp Ser His Thr
         35
                                                                   165
gaa ttc agg cct ttc agc tta
Glu Phe Arg Pro Phe Ser Leu
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<212> PRT
<213> Helicobacter pylori
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Lys Glu Leu Leu Asn Asn His Phe Lys Gln Arg Leu Ala Phe Arg Cys
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Asn Gly Glu Asn Leu Ser Ala Ile Lys Lys Asp Leu Pro Leu Leu Thr
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Asn Glu Leu Asn Ala Leu Phe Val Glu Leu Ser Lys Asp Ser His Thr
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 Thr Ser Leu Asn Lys Leu Ile Tyr Thr Gly Gln Ile Ile Pro Asp Arg
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  1
 ggt teg tgg ttg tat ttt gaa tac gat tet aaa gat gtt tta tac get
 Gly Ser Trp Leu Tyr Phe Glu Tyr Asp Ser Lys Asp Val Leu Tyr Ala
 cgt atc aat aaa cgc cgt aaa gtg cct gtt acc att tta ttc agg gcg
 Arg Ile Asn Lys Arg Arg Lys Val Pro Val Thr Ile Leu Phe Arg Ala
                              40
 atg gat tat caa aaa caa gac atc atc aaa atg ttc tac ccg ctt gtt
 Met Asp Tyr Gln Lys Gln Asp Ile Ile Lys Met Phe Tyr Pro Leu Val
 aaa gtg cgt tat gaa aac gat aaa tat ttg atc ccg ttt gct tca tta
 Lys Val Arg Tyr Glu Asn Asp Lys Tyr Leu Ile Pro Phe Ala Ser Leu
                                        . 75
                      70
 65
 gac gcc aat caa aga atg gaa ttt gac ttg aaa gat cct caa ggc aag
                                                                    288
 Asp Ala Asn Gln Arg Met Glu Phe Asp Leu Lys Asp Pro Gln Gly Lys
```

								•								
				85					90					95		
att	att	ctt	tta	aca	aat	aaa	aag	ctc	act	tca	aga	aag	att	aaa	gag	336
Val	Ile	Leu	Leu 100	Ala	ĞÎy	Lys	Lys	Leu 105	Thr	Ser	Arg	Lys	Ile 110	Lys	Glu	
		gaa	200	cat	tta	паа	taa	ata	gaa	tac	cct	atg	gat	att	tta	384
Tou	Tue	Glu	Aen	His	Leu	Glu	Trp	Val	Glu	Tyr	Pro	Met	Asp	Ile	Leu	
		115					120					125				420
ctc	aat	cgc	cat	tta	gct	gag	cct	gtt	atg	gta	ggg	aaa	gaa	gtc	tta	432
Leu	Asn	Arg	His	Leu	Ala	Glu 135	Pro	Val	Met	Val	140	rys	GIU	vaı	ьeu	
tta	σac	atg	ctc	act	cag	cta	gat	aaa	aac	aaa	tta	gaa	aaa	atc	cac	480
Leu	Asp	Met	Leu	Thr	Gln	Leu	Asp	Lys	Asn	Lys	Leu	Glu	Lys	Ile	HIS	
145	_				150					155					TOU	
+	tta	ggc	gtg	caa	gaa	ttt	gtg	atc	atc	aac	gat	ctg	gcg	tta	ggg	528
Asp	Leu	Gly	Val	Gln	Glu	Phe	Val	Ile	Ile	Asn	Asp	Leu	Ala	Leu	Gly	
				165					170					1/2		
cat	gac	gct	tcc	att	atc	caa	tct	ttt	tca	gcc	gat	tct	gag	tct	ttg	576
His	Asp	Ala	Ser	Ile	Ile	Gln	Ser	Phe	Ser	Ala	Asp	Ser	Glu	Ser	Leu	
			180					185					190			
222	tta	ctc	aag	caa	acc	gaa	aaa	att	gat	gat	gaa	aac	gct	cta	gcg	624
Lys	Leu	Leu	Lys	Gln	Thr	Ğlu	Lys 200	Ile	Asp	Asp	Glu	Asn 205	Ala	Leu	Ala	•
		195 cgt				att		222	cca	aac	gat		att	acq	act	672
gcg	att	Arg	TIO	uic	Tue	Val	Met	Lvs	Pro	Glv	Asp	Pro	Val	Thr	Thr	
Ala		Arg	TTE	urs	цуз	215		270		<b>4-1</b>	220					
	210				+++	at c	222	222	ctt	ttc		σat	cca	gaa	cgc	720
gaa	gtg	gct	aag	Cay	Pho	Val	Luc	T.vs	Len	Phe	Phe	Asp	Pro	Glu	Arg	
	vaı	ATS	гÃ2	6111	230	<b>V</b> 0.1	2,5	-,0		235	• • • • • • • • • • • • • • • • • • • •				240	
225				. + ~	230	~~~	cac	atα	222		aat	cac	aaσ	tta	ggc	768
tat	gat	ttg	acc	Mot	ycy val	Glu	Ara	Met	Lvs	Met	Asn	His	Lvs	Leu	Gly	
Tyr	Asp	Leu	The		vaı	GIY	nry		250				-,,-	255		
				245	+ 20	att	200	act		acq	cat	σаа	gat		atc	816
ttg	cat	gtg	CCL	yat	Tir	Tla	Thr	Thr	Len	Thr	His	Glu	Asp	Ile	Ile	
Leu	HIS	var			1 1 1	110		265					270			
		gtt	260		at a	ata	220		222	aac	aat	ca				854
acc	acc	Val	aaa	m	Ton	Mat	Lvs	Tle	Lvs	Asn	Asn					
Thr	Thr	275	гуз	ıyı	Den	He C	280		2,2							
<b>c</b> 21	0> 7															
	1> 2															
_	2> P															
		elic	obac	ter	pylo	ri										
-40	n 7	Ω		•												
Thr	Ser	Leu	Asn	Lys	Leu	Ile	Tyr	Thr	Gly	Gln	Ile	Ile	Pro	Asp	Arg	
1				- 5					10					13		
Gly	Ser		20					25					30		Ala	
7-0	Tla	Acn	Lvs	Ara	Ara	Lvs	Val	Pro	Val	Thr	Ile	Leu	Phe	Arg	Ala	
ALG	110	35		9	5	-4-	40					45	ı			
Met	Asp	Tvr	Gln	Lys	Gln	Asp	Ile	Ile	Lys	Met	Phe	Tyr	Pro	Leu	Val	
	50					55					60					
T.vs	. Val	Ara	Tvr	Glu	Asn	Asp	Lys	Tyr	Leu	Ile	Pro	Phe	Ala	Ser	Leu	
65					70					75					80	
Asp	Ala	Asn	Gln			Glu	Phe	Asp	Leu 90	Lys	Asp	Pro	Gln	Gly 95	Lys	
		_	-	85	ci.	T	T	T.ev			<b>Δ</b> ~~	Lve	710			
Val	Ile	Leu			сту	гÀ2	nys	105	****	261	9	y	110		Glu	
			100		•	C1	m			Ψ	D=^	Mot			ום.]	
Lev	Lys			HIS	Leu	GIU	110	AGT	GIU	+ A T	LLO	125	. Aug		Leu	
		115		_		<b>61</b>	120		Mar	W-1	G1			V=1	וים, ז	
Lev			His	Leu	Ala			val	mec	AGI	140	- Lys	GIU	. 491	Leu	
	130	)	_			135	n	7	N	T			Term	710	ніе	
Let	Asp	Met	Leu	Thr	GID	ьeи	ASP	ъyS	H211	ьys	Ten	GIU	. nys		His	

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155
                    150
Asp Leu Gly Val Gln Glu Phe Val Ile Ile Asn Asp Leu Ala Leu Gly
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His Asp Ala Ser Ile Ile Gln Ser Phe Ser Ala Asp Ser Glu Ser Leu
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Lys Leu Leu Lys Gln Thr Glu Lys Ile Asp Asp Glu Asn Ala Leu Ala
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                            200
Ala Ile Arg Ile His Lys Val Met Lys Pro Gly Asp Pro Val Thr Thr
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                        215
Glu Val Ala Lys Gln Phe Val Lys Lys Leu Phe Phe Asp Pro Glu Arg
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                                        235
Tyr Asp Leu Thr Met Val Gly Arg Met Lys Met Asn His Lys Leu Gly
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                245
Leu His Val Pro Asp Tyr Ile Thr Thr Leu Thr His Glu Asp Ile Ile
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agg gat tot tgg gga gcg atc aaa gcc aat cgc gca ggc gtt gta gaa
                                                                   96
Arg Asp Ser Trp Gly Ala Ile Lys Ala Asn Arg Ala Gly Val Val Glu
aaa att gat tot aaa aat att tat att tta ggc gaa agc aaa gaa gaa
Lys Ile Asp Ser Lys Asn Ile Tyr Ile Leu Gly Glu Ser Lys Glu Glu
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         35
gcc tat att gat gcg tat tct ttg caa aaa aac ttg cgc acc aac caa
                                                                    192
Ala Tyr Ile Asp Ala Tyr Ser Leu Gln Lys Asn Leu Arg Thr Asn Gln
                                              60
                         55
aac acc agt ttc aat caa gtc cct atc gtt aaa gtg ggc gat aaa gtg
                                                                    240
Asn Thr Ser Phe Asn Gln Val Pro Ile Val Lys Val Gly Asp Lys Val
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gga gcc ggg caa atc atc gct gat ggc cct agc atg gat aga ggc gag
                                                                    288
Gly Ala Gly Gln Ile Ile Ala Asp Gly Pro Ser Met Asp Arg Gly Glu
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ttg gcg tta ggg aaa aat gtg cgc gtg gcg ttc atg cct tgg aat ggc
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Leu Ala Leu Gly Lys Asn Val Arg Val Ala Phe Met Pro Trp Asn Gly
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tat aac ttt gaa gac gcg atc gtg gtg agt gag tgc atc act aaa gat
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Tyr Asn Phe Glu Asp Ala Ile Val Val Ser Glu Cys Ile Thr Lys Asp
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                            120
gat att ttc act tcc acc cac att tat gaa aaa gaa gtg gat gct agg
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Asp Ile Phe Thr Ser Thr His Ile Tyr Glu Lys Glu Val Asp Ala Arg
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                        135
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gag ctt aag cat ggt gtg gaa gaa ttt acc gct gat att cct gat gtg
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Glu Leu Lys His Gly Val Glu Glu Phe Thr Ala Asp Ile Pro Asp Val
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                    150
aaa gaa gaa gcg ctc gct cat ctt gat gaa agc ggg atc gtt aaa gtc
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Lys Glu Glu Ala Leu Ala His Leu Asp Glu Ser Gly Ile Val Lys Val
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Lys	Leu	Ser	Ile	Leu	Glu	Lys	Asp 360	Asp	116	ren	Pro	365	GIY	Val	116	
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cat	t act	aaa	ato	cta	gaa	ato	; gct	aac	gct	att	aat	gaa	aaa	a gad	c écc	1440
Are	g Álá	a Lys	Met	: Let	Glu	ı Ile	Ala	Ası	Ala	TTE	: Mai	GIU	ı r.ys	s Asp		
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tte	g aca	a ato	cat	gc	ctt	gaç	aat	: tgt	tct	. gat	gaa	gaç	CEL	. LTS	gaa	1400
Le	u Thi	r Ile	e His	s Ala	Leu ;	ı Glı	ı Asr	ı Cys	490	) Hal	GI	GIC	ı De	49	5	
+ =	ם מכי	a aa	a gat			aad	ggg	gtt	aaq	ato	g gct	: ato	cct	gt	ttt Dhe	1536
Tu.	r Ala	LV	s Ast	o Tri	Sei	Lys	Gly	/ Val	Lys	: Mėt	Ala	ıle	EL	ya.	l Phe	
			500	ገ				ວບ:	)				311	,		1584
ga	a gg	c ato	tc	g caa	a gaa	aaa	a ttt	tat	aaq	CE	י בבו	. gaa	1 LT	a ge	t aag	1304

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aaa	atg Met	agg	gag	cgc	gra	aat Aan	y - y	Glu	Tur	Mot	Tur	Met	Tle	Lvs	Leu	
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GIII	MIG		Gry	014			600					605	_	_		
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ATA		116	wah	ALG	- 7 -	55			-1-		60	•				
	50 Thr	C	Dho	) an	Gl n	Val	Pro	Tle	Val	I.vs	Val	Glv	Asp	Lys	Val	
	Thr	Ser	Pne	Maii	70	VOI	110			75		2	•	•	80	
65				~1.	70	21.	7.00	Clu	Pro		Met	Asn	Ara	Glv	Glu	
Gly	Ala	GTA	GIn		TIE	WIG	иор	GLY	90	561				95		
				85	_		_	•••		nh-	Mot	Dwo	Ф~~		Glv	
Leu	Ala	Leu	Gly	Lys	Asn	vai	Arg	vai	WIS	Pile	Mec	FIO	110	HOII	013	
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Asp	Ile	Phe	Thr	Ser	Thr	His	Ile	Tyr	Glu	Lys	Glu	Val	Asp	Ala	Arg	
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Glu	Leu	Lvs	His	Gly	Val	Glu	Glu	Phe	Thr	Ala	Asp	Ile	Pro	Asp	Val	
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Ive	Glu	Glu	Ala	Leu	Ala	His	Leu	Asp	Glu	Ser	Gly	Ile	Val	Lys	Val	
гуз	GIU	GIU	*****	165		•		•	170					175		
<b>63</b>	Thr	m	17-1	Sor	λla	Glv	Met	Tle		Val	Glv	Lvs	Thr	Ser	Pro	
GTA	Thr	Tyr			VIG	013		185			2		190		•	
	Gly		180	•	C	mh-	Dro		Glu	Ara	ī.en	Ī. <b>6</b> 11			Ile	
Lys	GLA		TTE	гàг	ser	1111	LIO	GIU	GIU	my		205	7			
		195				•	200	**- 3	<b>3</b>	T	C		T	Cue	Dro	
Phe	Gly	Asp	Lys	Ala	Gly	His	var	vaı	ASN	гÀг	Set	nea	ıyı	Cys	Pro	
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Pro	Ser	Leu	Glu	Gly	Thr	Val	Ile	Asp	Val	Lys	Val	Phe	Thr	ьys	гÀг	
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61"	Tyr	Glii	Lvs	Aso	Ala	Ara	Val	Leu	Ser	Ala	Tyr	Glu	Glu	Glu	Lys	
GIY	- 1 -		-1-	245		- 3			250		_			255		
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ATS	ьÀЗ	Leu	260					265	9			_	270		-	
	Glu	T	7 000	2	V-1	Ser	Ser		Į.e.i	Ser	Gln	Ala	Ile	Leu	Glu	
Glu	GIU			arg	AGT	261	280					285				
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Ser Leu Val Thr His Gln Pro Val Gly Gly Lys Ala Leu Phe Gly Gly
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Cys	Phe	Lys		Arg	Thr	Ser	Phe		Arg	Leu	гля	Tyr	_eu	Asn	116	
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gaa	gtg	atc	aat	gat	Cat	ggt	Tle	Gln	Ser	ī.vs	His	Met	Lvs	gac Asp	Phe	00.
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Gln	Phe	Lys	Val		vaı	PIQ	vaı	GTÀ	330	Asp	116	POII	III	Lys 335	Gru	
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                                                  45
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Ser Asn Lys Ser Val Glu Thr Ile Lys Glu Leu Ile Leu Asn Ser Ile
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gae tet tat aac ace ttt gat caa tac etc tat aac tta tgg gat age
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Asp Ser Tyr Asn Thr Phe Asp Gln Tyr Leu Tyr Asn Leu Trp Asp Ser
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tet tet gtt tat cat age aaa tgg gtg egt eet gte tta gee eta get
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_	L> 13															
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Glu	Phe	Glu	Ser	Val	Phe	Ser	Ala	IIe	vaı	PIO	Leu	GIU	wab	тeп	тэр	
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<pre>400 Leu 1 Ile Asp Ser Leu 65 Gly Asp Val</pre>	O> 90 Val Lys Gly Asp 50 Leu Glu Phe Lys	Ser Lys Tyr 35 Ser Ser Asp Ile Glu 115	Ser Thr 20 Asp Pro Lys Ile Tyr 100 Leu	Ser 5 Glu Phe Val Asp Ile 85 Ala Phe	Glu Leu Arg Glu 70 Leu Tyr	Tyr Lys Lys Met 55 Glu Asp Lys Ser	Gln Glu 40 Tyr Ile Ala Asp Phe 120	Lys 25 Lys Leu Glu Ile Ala 105 Asp	10 Val Asp Arg Leu Cys 90 Leu Asp	Leu Phe Glu Ser 75 Ser Ile Asp	Asp Leu Met 60 Lys Val Asn Asp	Glu 45 Gly Gln Pro Arg Glu 125	Glu 30 Trp Asp Ile Tyr Glu 110 Asn	Ser Ile Arg Leu 95 Arg Ser	Glu Arg Lys Leu 80 Ile Arg Val	
<pre>400 Leu 1 Ile Asp Ser Leu 65 Gly Asp Val Ser</pre>	D> 90 Val Lys Gly Asp 50 Leu Glu Phe Lys Asp	Ser Lys Tyr 35 Ser Ser Asp Ile Glu 115 Ser	Ser Thr 20 Asp Pro Lys Ile Tyr 100 Leu Lys	Ser 5 6 1u Phe Val Asp 11e 85 Ala Phe Lys	Glu Leu Arg Glu 70 Leu Tyr Arg	Tyr Lys Lys Met 55 Glu Asp Lys Ser Glu 135	Gln Glu 40 Tyr Ile Ala Asp Phe 120 Asp	Lys 25 Lys Leu Glu Ile Ala 105 Asp	10 Val Asp Arg Leu Cys 90 Leu Asp	Leu Phe Glu Ser 75 Ser Ile Asp Glu	Asp Leu Met 60 Lys Val Asn Asp	Glu 45 Gly Gln Pro Arg Glu 125 Glu	Glu 30 Trp Asp Ile Tyr Glu 110 Asn	Ser Ile Arg Leu 95 Arg Ser Asn	Glu Arg Lys Leu 80 Ile Arg Val Glu	
Leu 11 11e Asp Ser Leu 65 Gly Asp Val Ser Glu	D> 90 Val Lys Gly Asp 50 Leu Glu Phe Lys Asp	Ser Lys Tyr 35 Ser Ser Asp Ile Glu 115 Ser	Ser Thr 20 Asp Pro Lys Ile Tyr 100 Leu Lys	Ser 5 6 1u Phe Val Asp 11e 85 Ala Phe Lys	Glu Leu Arg Glu 70 Leu Tyr Arg Asp	Tyr Lys Lys Met 55 Glu Asp Lys Ser	Gln Glu 40 Tyr Ile Ala Asp Phe 120 Asp	Lys 25 Lys Leu Glu Ile Ala 105 Asp	10 Val Asp Arg Leu Cys 90 Leu Asp	Leu Phe Glu Ser 75 Ser Ile Asp Glu	Asp Leu Met 60 Lys Val Asn Asp	Glu 45 Gly Gln Pro Arg Glu 125 Glu	Glu 30 Trp Asp Ile Tyr Glu 110 Asn	Ser Ile Arg Leu 95 Arg Ser Asn	Glu Arg Lys Leu 80 Ile Arg Val Glu	
<pre>400 Leu 1 Ile Asp Ser Leu 65 Gly Asp Val Ser Glu 145</pre>	O> 90 Val Lys Gly Asp 50 Leu Glu Phe Lys Asp 130 Arg	Ser Lys Tyr 35 Ser Ser Asp Ile Glu 115 Ser Lys	Ser Thr 20 Asp Pro Lys Ile Tyr 100 Leu Lys	Ser 5 Glu Phe Val Asp Ile 85 Ala Phe Lys Val Phe	Glu Leu Arg Glu 70 Leu Tyr Arg Asp Val	Tyr Lys Lys Met 55 Glu Asp Lys Ser Glu 135	Glu 40 Tyr Ile Ala Asp Phe 120 Asp	Lys 25 Lys Leu Glu 11e Ala 105 Asp Asn	10 Val Asp Arg Leu Cys 90 Leu Asp Glu Asp	Leu Phe Glu Ser 75 Ser Ile Asp Glu Lys 155	Asp Leu Met 60 Lys Val Asn Asp 140 Lys	Glu 45 Gly Gln Pro Arg Glu 125 Glu	Glu 30 Trp Asp Ile Tyr Glu 110 Asn Glu Val	Ser Ile Arg Leu 95 Arg Ser Asn Glu	Glu Arg Lys Leu 80 Ile Arg Val Glu Lys 160	
Asp Ser Leu 65 Gly Asp Val Ser Glu 145 Val	O> 90 Val Lys Gly Asp 50 Leu Glu Phe Lys Asp 130 Arg	Ser Lys Tyr 35 Ser Ser Asp Ile Glu 115 Ser Lys Glu	Ser Thr 20 Asp Pro Lys Ile Tyr 100 Leu Lys Lys Ser Glu	Ser 5 6 1u Phe Val Asp 11e 85 Ala Phe Lys Val Phe 165	Glu Leu Arg Glu 70 Leu Tyr Arg Asp Val 150 Lys	Tyr Lys Lys Met 55 Glu Asp Lys Ser Glu 135 Ser	Glu 40 Tyr Ile Ala Asp Phe 120 Asp Glu Leu	Lys 25 Lys Leu Glu Ile Ala 105 Asp Asn Lys	10 Val Asp Arg Leu Cys 90 Leu Asp Glu Asp Lys 170	Leu Phe Glu Ser 75 Ser Ile Asp Glu Lys 155 Ala	Asp Leu Met 60 Lys Val Asn Asp 140 Lys	Glu 45 Gly Gln Pro Arg Glu 125 Glu Arg Lys	Glu 30 Trp Asp Ile Tyr Glu 110 Asn Glu Val Glu	Ser Ile Arg Leu 95 Arg Ser Asn Glu Trp	Glu Arg Lys Leu 80 Ile Arg Val Glu Lys 160 Leu	
Asp Ser Leu 65 Gly Asp Val Ser Glu 145 Val Lys	D> 90 Val Lys Gly Asp 50 Leu Glu Phe Lys Asp 130 Arg Gln Ala	Ser Lys Tyr 35 Ser Ser Asp Ile Glu 115 Ser Lys Glu Leu	Ser Thr 20 Asp Pro Lys Ile Tyr 100 Leu Lys Lys Ser Glu 180	Ser 5 Glu Phe Val Asp Ile 85 Ala Phe Lys Val Phe 165 Ala	Glu Leu Arg Glu 70 Leu Tyr Arg Asp Val 150 Lys	Tyr Lys Lys Met 55 Glu Asp Lys Ser Glu 135 Ser Ala Ile	Glu 40 Tyr Ile Ala Asp Phe 120 Asp Glu Leu Asp	Lys 25 Lys Leu Glu Ile Ala 105 Asp Asn Lys Asp Glu 185	10 Val Asp Arg Leu Cys 90 Leu Asp Glu Asp Lys 170 Arg	Leu Phe Glu Ser 75 Ser Ile Asp Glu Lys 155 Ala Glu	Asp Leu Met 60 Lys Val Asn Asp 140 Lys Lys	Glu 45 Gly Gln Pro Arg Glu 125 Glu Arg Lys Glu	Glu 30 Trp Asp Ile Tyr Glu 110 Asn Glu Val Glu Leu 190	Ser Ile Arg Leu 95 Arg Ser Asn Glu Trp 175 Val	Glu Arg Lys Leu 80 Ile Arg Val Glu Lys 160 Leu Arg	
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Ala Gln Val Pro Glu Ala Thr Met Val Ser Val Tyr Met Asp Leu Lys 275  Lys Leu Phe Leu Thr Lys Glu Ala Ser Glu Glu Gly Phe Asp Leu Ala 290  Pro Asn Lys Leu Lys Glu Ile Leu Glu Gln Ile Lys Arg Gly Lys Leu 305  Ile Ser Asp Arg Ala Lys Asn Lys Met Ala Lys Ser Asn Leu Arg Leu 325  Val Val Ser Ile Ala Lys Arg Phe Thr Ser Arg Gly Leu Pro Phe Leu 340  Asp Leu Ile Gln Glu Gly Asn Ile Gly Leu Met Lys Ala Val Asp Lys 355  Phe Glu His Glu Lys Gly Phe Lys Phe Ser Thr Tyr Ala Thr Trp Trg 370  Ile Lys Gln Ala Ile Ser Arg Ala Ile Ala Asp Gln Ala Arg Thr Ile Ala Asp Asp Gln Ala Arg Thr Ile Ala Asp Asp Care Asp Ala Ile Ala Asp Asp Care Asp Ala Asp	s a u 0
275 Lys Leu Phe Leu Thr Lys Glu Ala Ser Glu Glu Gly Phe Asp Leu Ala 290 Pro Asn Lys Leu Lys Glu Ile Leu Glu Gln Ile Lys Arg Gly Lys Leu 305 Ile Ser Asp Arg Ala Lys Asn Lys Met Ala Lys Ser Asn Leu Arg Leu 325 Val Val Ser Ile Ala Lys Arg Phe Thr Ser Arg Gly Leu Pro Phe Leu 340 Asp Leu Ile Gln Glu Gly Asn Ile Gly Leu Met Lys Ala Val Asp Lys 355 Phe Glu His Glu Lys Gly Phe Lys Phe Ser Thr Tyr Ala Thr Trp Trg 370 Ile Lys Gln Ala Ile Ser Arg Ala Ile Ala Asp Gln Ala Arg Thr Ile	a u 0
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325 Val Val Ser Ile Ala Lys Arg Phe Thr Ser Arg Gly Leu Pro Phe Leu 340 Asp Leu Ile Gln Glu Gly Asn Ile Gly Leu Met Lys Ala Val Asp Lys 355 Phe Glu His Glu Lys Gly Phe Lys Phe Ser Thr Tyr Ala Thr Trp Trg 370 Ile Lys Gln Ala Ile Ser Arg Ala Ile Ala Asp Gln Ala Arg Thr Ile	u
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370 375 380  Ile Lys Gln Ala Ile Ser Arg Ala Ile Ala Asp Gln Ala Arg Thr Ile	
306 330	·V
Arg Ile Pro Ile His Met Ile Asp Thr Ile Asn Arg Ile Asn Lys Val 405 410 415	
Met Arg Lys His Ile Gln Glu Asn Gly Lys Glu Pro Asp Leu Glu Val 420 425 430	
Val Ala Glu Glu Val Gly Leu Ser Leu Asp Lys Val Lys Asn Val IIe 435 440 445	
Lys Val Thr Lys Glu Pro Ile Ser Leu Glu Thr Pro Val Gly Asn Asp 450 450 450 450 450 460 450 460	
Asp Asp Gly Lys Phe Gly Asp Phe Val Glu Asp Lys Asn Ile Val Ser 465 470 475 486	10
Ser Ile Asp His Ile Met Arg Glu Asp Leu Lys Ala Gln Ile Glu Ser  485 490 495 495	
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Phe Gly Leu Leu Asp Asp Glu Ser Asp Arg Thr Leu Glu Glu Ile Gl 515 520 525 Lys Glu Leu Asn Val Thr Arg Glu Arg Val Arg Gln Ile Glu Ser Se	
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- 1 5 15 15 15 15 15 15 15 15 15 15 15 15	
gaa tta gag gat ttg tat cac gaa ttc agt gaa gat aag cgt tct at Glu Leu Glu Asp Leu Tyr His Glu Phe Ser Glu Asp Lys Arg Ser Il 20 25 30	le
20 20 and and goo car as ago go sat gar at got as gog gt	tg 144
Phe Tyr Phe Ala Pro Thr Asn Ala His Lys Asp Met Leu Lys Ala Va	a.L
gat ttt ttc aaa gaa aaa ggt cat acg gct tat tta gat gag gtg ag Asp Phe Phe Lys Glu Lys Gly His Thr Ala Tyr Leu Asp Glu Val Ar	gg 192

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gaa tac aaa acc tta gag cct tta aaa agc cta gaa atc cgt ttg agt
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Glu Tyr Lys Thr Leu Glu Pro Leu Lys Ser Leu Glu Ile Arg Leu Ser
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gaa gee eec att gat aaa ege aat gat ttt tta tae eat aag aee aet
Glu Ala Pro Ile Asp Lys Arg Asn Asp Phe Leu Tyr His Lys Thr Thr
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tat gcc cct ttt tat caa aag gct cga gcg ctc att aaa aag ggc gtt
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Tyr Ala Pro Phe Tyr Gln Lys Ala Arg Ala Leu Ile Lys Lys Gly Val
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atg ttt gat gaa atc ttt tat aac cag gat ttg gaa ctc act gag ggc
                                                                   240
Met Phe Asp Glu Ile Phe Tyr Asn Gln Asp Leu Glu Leu Thr Glu Gly
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                     70
get agg age aat ett gtt tta gaa ate eat aac agg ett tta ace eet
                                                                    288
Ala Arg Ser Asn Leu Val Leu Glu Ile His Asn Arg Leu Leu Thr Pro
                 85
tat ttt agc gcg ggc gcg tta aac ggg acg ggt gtt gtg ggg ttg tta
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Tyr Phe Ser Ala Gly Ala Leu Asn Gly Thr Gly Val Val Gly Leu Leu
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            100
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Lys Lys Gly Leu Val Gly His Ala Pro Leu Lys Leu Gln Asp Leu Gln
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Tyr Ala Pro Phe Tyr Gln Lys Ala Arg Ala Leu Ile Lys Lys Gly Val
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Met Phe Asp Glu Ile Phe Tyr Asn Gln Asp Leu Glu Leu Thr Glu Gly
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Ala Arg Ser Asn Leu Val Leu Glu Ile His Asn Arg Leu Leu Thr Pro
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Tyr Phe Ser Ala Gly Ala Leu Asn Gly Thr Gly Val Val Gly Leu Leu
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            100
Lys Lys Gly Leu Val Gly His Ala Pro Leu Lys Leu Gln Asp Leu Gln
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 aaa ata gat tgg caa aaa gat tat gac agg gaa aaa tta gaa cga gat
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 Asn Arg Asp Leu Glu Gln Cys Lys Glu Asp Leu Leu Ala Ala Asn Glu
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                             40
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 Asn Leu Arg Asn Arg Ile Gln Glu Trp Glu Asn Glu Lys Asn Lys Leu
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                         55
 Asp Pro Arg Asp Glu Arg Ile Lys Glu Leu Glu Glu Glu Lys Arg Glu
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 tta gag gga att tta gcc caa aaa gag aac gca gaa caa aaa tat aac
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                  85
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 Thr Leu Ser Val Lys Asn Lys Gln Leu Glu Ala Glu Leu Asp Met Leu
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             100
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 Asn Glu Lys Phe Glu Lys Leu Lys Asn Met Tyr Ala Gly Val Glu Asp
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 Phe Glu Lys Arg Gln Lys Asn Ile Lys Glu Gln Ile Val Lys Thr Asn
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                        135
 ccc aaa gtc tta ggc gca cct tca aac gaa gtg gaa gaa tta gcg ttc
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  Pro Lys Val Leu Gly Ala Pro Ser Asn Glu Val Glu Glu Leu Ala Phe
  tta gag cgt ata gaa aag ggc atg caa gag ttc aat gtt ttc tat ccc
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gct gtg cag cct act tgg gat agc cca gaa tcg ttg atg ggg tat tt
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Thr Leu Ser Val Lys Asn Lys Gln Leu Glu Ala Glu Leu Asp Met Leu
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                            120
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Phe Glu Lys Arg Gln Lys Asn Ile Lys Glu Gln Ile Val Lys Thr Asn
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Pro Lys Val Leu Gly Ala Pro Ser Asn Glu Val Glu Glu Leu Ala Phe
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Lys Arg Leu Leu Tyr Met Phe His Thr Ala Leu Lys Ser Thr Ser Leu
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Leu Pro Lys Leu Tyr Val His Phe Gly Gly Leu Asn Phe Leu Ser Ile
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Leu Asp Gln Ala Pro Ile Gly Lys Thr Pro Arg Ser Asn Pro Ala Thr
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Tyr	Thr	Gly	Val	Met	Asp	Glu	Ile	Arg	He	Leu	Pne	45	GIU	GIH	rys	
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gaa	gct	aaa	att	tta	ggc	tat	agt	gcg	Sor	Ara	Dhe	Ser	Phe	Asn	Val	
Glu		Lys	Ile	Leu	GIĀ	Tyr 55	Ser	HIG	Ser	ALY	60	001				
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65					70					15					00	
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Glu	Met	His	Phe	Leu	Pro	Ásp	Val	Leu	Val	Gln	Суѕ	Asp	Ser	Cys	Lys	
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Gly	Āla	Lys	Tyr	Asn	Pro	Gln	Thr	Leu	Glu	Ile	Lys	vaı	110	GTĀ	гÀг	
			100					105			~~~	~a+		~==	+++	384
tcc	att	gcc	gat	gtg	ttg	aac	atg	agc	geg.	gaa Clu	Glu	Ala	Tyr	Glu	Phe	501
Ser	Ile		Asp	Val	Leu	Asn	120	Ser	Val	GIU	GIU	125	-1-			
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TTT	gct	Tve	Dhe	Pro	I.vs	Tle	Ala	Val	Lvs	Leu	Lys	Thr	Leu	Met	Asp	
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ata		tta	aac	tat	atc	act	tta	ggg	caa	aac	gct	acg	act	tta	agt	480
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1 4 5					150	,				122					100	500
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Gly	Gly	Glu	Ala	Gln	Arg	Ile	Lys	Leu	ATa	гÀг	GIU	reu	Ser	175	гуэ	
				165					170	~~~	cct	act	acc		tta	576
gac	aca	ggc	aaa	acc	CTT	Tat	Tla	LLa) ac	Glu	Pro	Thr	Thr	Glv	ttg Leu	• • •
Asp	Thr	GTA	Lуs 180	THE	Leu	ıyı	116	185	nop	01			190			
		~ 33	asc.	ata	aat	cat	ctt	tta	caa	qtc	ttg	cat	tct	tta	gtg	624
Uic	Dhe	Glu	Asp	Val	Asn	His	Leu	Leu	Gln	Val	Leu	His	Ser	Leu	Val	•
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Ala	Leu	Gly	Asn	Ser	Met	Leu	Val	Ile	Glu	His	Asn	Leu	Asp	Пе	Ile	
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ggc	999	aaa	y.c	Tla	Ala	Ser	Glv	Thr	Pro	Leu	Glu	Val	Āla	Glr	Asn	
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tac	даа	aaa	acc	caa	ago	tac	acg	gga	aaa	ttt	tta	gct	ttg	gaa	ttg	816
Cvs	Glu	Lys	Thr	Gln	Ser	Tyr	Thr	Gly	Lys	Phe	Leu	Ala	. rea	GIU	Leu	
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aaa	ı															819
Lys	;															
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1				5	1				10					1.	,	
נ יים.ז	Asr	Gln	Ala	Pro	Ile	Gly	Lys	Thr	Pro	Arg	Ser	Asn	Pro	Ala	Thr	
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Tvr	Thr	Glv	Val	Met	Asp	Glu	Ile	Arg	Ile	Leu	Phe	Ala	Glu	Glr	l Lys	
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Gly Ala Lys Tyr Asn Pro Gln Thr Leu Glu Ile Lys Val Lys Gly Lys
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Gly Gly Glu Ala Gln Arg Ile Lys Leu Ala Lys Glu Leu Ser Lys Lys
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His Phe Glu Asp Val Asn His Leu Leu Gln Val Leu His Ser Leu Val
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Ala Leu Gly Asn Ser Met Leu Val Ile Glu His Asn Leu Asp Ile Ile
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Lys Asn Ala Asp Tyr Ile Ile Asp Met Gly Pro Asp Gly Gly Asp Lys
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Lys Ser Gly Glu Pro Tyr Ile Val His Pro Ile Cys Val Ala Ser Leu
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aaa Tuo	Clu	Thr	T.AII	Ala	Val	Tvr	Ala	Pro	Ile	Ala	Ser	Arg	Leu	Gly	Met	
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Tyr	Gly	Asn	Ser	Ala	HIS	ırp	гÃ2	Tyr	гÃа	WIG	GIY	365	AGT	rap	1113	
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Glu	_	His	HIS	GIU	GIY		ALG	пр	TEA	GIII	380	LIIC	טעט	-1-		
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Asn	Asp	ren	TAT		GIU	voħ	110	141	410	1110	-	•		415		
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act	tac	acc	Tan	Pro	y . y	Glu	Bla	Tle	Δla	Len	Asp	Phe	Ala	Tvr	Met	
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aaa	aaa	gcc	LLd	Leu	Aer	Cay	Gli	Len	Arc	Ser	C) n	Asp	Val	Val	Lvs	
гÀг		WIG	neu.	neu	HOII	455	Ų.LU	a-cu	••• 9		460					
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1405

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                           120.
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Lys Glu Thr Leu Ala Val Tyr Ala Pro Ile Ala Ser Arg Leu Gly Met
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Ser Ser Ile Lys Asn Glu Leu Glu Asp Lys Ser Phe Tyr Tyr Ile Tyr
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Pro Glu Glu Tyr Lys Asn Ile Lys Glu Tyr Leu His Lys Asn Lys Gln
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Ser Leu Leu Leu Lys Leu Asn Ala Phe Ala Ser Lys Leu Glu Lys Lys
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Leu Phe Asp Ser Gly Phe Ser His Ser Asp Phe Lys Leu Val Thr Arg
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Val Lys Arg Pro Tyr Ser Ile Tyr Leu Lys Met Gln Arg Lys Gly Ala
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Val Asn Ile Asp Glu Ile Leu Asp Leu Leu Ala Ile Arg Ile Leu Leu
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                            280
Lys Asn Pro Ile Asp Cys Tyr Lys Val Leu Gly Ile Ile His Leu Asn
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Phe Lys Pro Ile Val Ser Arg Phe Lys Asp Tyr Ile Ala Leu Pro Lys
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                    310
Glu Asn Gly Tyr Lys Thr Ile His Thr Thr Ile Phe Asp Glu Ser Ser
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                325
Val Tyr Glu Val Gln Ile Arg Thr Phe Asp Met His Met Gly Ala Glu
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Tyr Gly Asn Ser Ala His Trp Lys Tyr Lys Ala Gly Gly Val Asp His
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Glu Asp His His Glu Gly Met Arg Trp Leu Gln Asn Phe Lys Tyr His
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Asp Ser Asp Leu Lys Asn Asp Pro Lys Glu Phe Tyr Glu Leu Ala Lys
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Val His Ser Asp Leu Gly Asp Lys Ala Thr Asp Ala Tyr Ile Asn Ser
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Arg Ile Ala Lys Ser Glu Leu Glu Lys Asp Thr Lys Leu Val Ser Ser
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His Asp Gln Tyr Glu Arg Met Lys Lys Ser Gly Ser Leu Asn Thr Glu
aac tta gat tcg cac att caa gcc aac agc tta caa gag ctg aat caa
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Asn Leu Asp Ser His Ile Gln Ala Asn Ser Leu Gln Glu Leu Asn Gln
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Lys Ala Val Gln Ile Ser Leu Asn Asn Pro Asn Leu Lys Asp Leu Glu
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                                                     110
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Arg Thr Lys Ala Leu Leu Lys Asp Cys Asp Val Val Phe Ile Ile Ser
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Ser Ser Asn Gln Phe Leu Thr Glu Ser Asp Met Ser Leu Phe Asp Arg
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His His His Gln Asp Asp Leu Ala Ile Gln Tyr Leu Pro Ala Val Arg
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cat	gtc	caa	aaa	gcg	Len	Acn	Gln	Met	Ser	Glu	Arg	Glu	Gln	Ile	Leu	
Hls	vaı	GIII	180	VIO	Dea	7.511	01	185					190			
		att	tat	tac	ttt	αаа	gag	tta	aat	ttg	agc	gag	att	aaa	gag	624
atc	Gla	T.e11	Tyr	Tvr	Phe	Glu	Glu	Leu	Asn	Leu	Ser	Glu	Ile	Lys	Glu	•
		1 9 5					200					203				
2++	tta	~~~	att	act	gaa	tcq	cgc	att	tct	caa	atc	att	aaa	gaa	gtg	672
Tle	Leu	Glv	Ile	Thr	Ğlu	Ser	Arg	Ile	Ser	Gln	Ile	Ile	Lys	Glu	Val	
	210					215					220					
att	222	ааσ	gtg	cgt	aaa	tcc	tta	gga	gtg	gat	cat	ggc				711
Ile	Lvs	Lys	Val	Arg	Lys	Ser	Leu	Gly	Val	Asp	His	Gly				
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<21	1> 2	37														
	.2> P															
<21	3> H	elic	obac	ter	pylo	ri										
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Ser	Glu	Lys	Asn	ITE	GIU	гуѕ	val	Leu	10	VIO	171	nop	_,_	15	Gln	
1				3		. 7	. 21-	Tla			Len	Pro	Ala			
His	His	His			Asp	reu	Ala	25	Gin	1 y L	ДСС		30	)	Arg	
_		~	20	7	. 7	T	Clu			Pro	Ser	Ser			Phe	
Ala	Met			Arg	ren	пуэ	40	, ,,,,,,	200			45		•		
_	_	35	) . 17-1	802	Tla	Gly			Glu	Leu	Ile			Ala	Arg	
Asr			1 A91	Ser	116	55		024			60				•	
_	50			. 21-	Tou	) Den	, Δen	Ser	Phe	Tro	Glv	Tvr	Ala	Lys	Thr	
		GIU	ı ser	MIG	70	, vor	i nop			75	,,	- 4 -		•	80	
65	•		C1.	. הות	Mot	Len	. Aen	ጥህን	Leu			Leu	Asp	Val	Ile	
Arg	y val	AST	י פדא	85 ×		. Den	. nop	-1-	90		,			95	5	
_	. •			. n	, T.++^	T.e.	Tle	j.ve			Asc	Ile	Glu		Thr	
Sei	Arg	, sei			nys	, בכנ		105					110	)		
		. 7 ^-	100	, , , , , , , , , , , , , , , , , , , ,	Hic	e G1 u	, I.va	Glu	Pro	Ser	Ast	Ala	Tyr	: Let	a Ala	
Lys	5 H15	ье. 115		. GIU		. 513	120	)				125				
<b>~1</b>	. m.	TT	, . G1.	, G1··	Den	Tle	Glu	Lvs	Ile	Lvs	Glu	Ala	Lys	Thi	Ala	
GLI	ı ını	Let	' OT?	GIU	. non					-,-			-			

	130					135					140					
C	Asp	T1.	Tur	Ala	T.e.ii	Val	Pro	Ile	Asp	Glu	Gln	Phe	Asn	Ala	Ile	
	Asp	TTE	ıyı	MIG		Vul				155					160	
145					150		_					C1	T	T		
Glu	Gln	Asp	Glu	Ile	Thr	Lys	Lys	lie	GIU	Ala	GIU	GIU	Leu	Leu	GIU	
				165					170					T/2		
Hie	Val	Gln	T.vs	Ala	Leu	Asn	Gln	Met	Ser	Glu	Arg	Glu	Gln	Ile	Leu	
III	101	02	180					185			-		190			
		_	100		D	C1	C1		n en	Lou	Sar	Glu		T.VS	Glu	
Ile	Gln	Leu	Tyr	Tyr	Pne	GIU	GIU	ren	ASII	Leu	Ser	205	116	Dy3	014	
		195					200					205	_			
Tle	Leu	Glv	Ile	Thr	Glu	Ser	Arg	Ile	Ser	Gln	Ile	Ile	Lys	Glu	Val	
	210	,				215	_				220					
_,	Lys	•	17-1	N	T		Len	Glv	Val	Asn	His	Glv				*
	Lys	гЛа	var	Arg		Ser	Dea	Gry	741	225		<b></b> 2				
225					230					235						
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	2> DI															
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	3> H	elico	ppaci	cer i	PATO	. 1										
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	2> (		(113	4)												
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<b>\4</b> 0	tac			a+ a		C22	cac	200	gag	cat	gat	tta	σaa	atq	att	48
gaa	tac	aac	ege	-	aaa	Caa	T	mb-	61	uic	) en	Ton	Glu	Mot	Tle	
Glu	Tyr	Asn	Arg	Leu	Lys	GIN	Arg	Thr	GIU	HIS	ASP	rea	GIU	1366	116	
1				5					10					15		
age	gcg	acc	aat	ata	tqt	aag	ggc	att	gaa	aat	tac	gcg	cgc	cat	ttc	96
50-	Ala	Thr	GIV	Vaĺ	Cvs	Lvs	Glv	Ile	Glu	Asn	Tyr	Ala	Arg	His	Phe	
Ser	WTG	1111	20		-,-	-1-	3	25			-		. 30			
			20							+ ~~	++4	+++		tat	tta	144
acc	ggt	aaa	gcc	CCT	aac	gaa	acg	CCL	-	Lyc	Z	Db -	3	m	Tou	
Thr	Gly	Lys	Ala	Pro	Asn	Glu	Thr	Pro	Phe	Cys	Leu	rne	ASP	Tyr	ren	
		35					40					45				
	att	+++	gag	caa	gag	ttt	tta	atc	att	qtg	gat	gaa	agc	cat	gtg	192
999	Ile	Db.	909	7	610	Dhe	Len	Val	Tle	νaί	Asp	Ğlu	Ser	His	Val	
GIA		Pne	GIU	ALG	GIU		Tierr	141	110	141	60		-,			
	50					55										240
agt	ttg	cca	cag	ttt	ggg	ggg	atg	tat	gca	ggg	gat	atg	agc	agg	aaa	240
Ser	Leu	Pro	Gln	Phe	Gly	Gly	Met	Tyr	Ala	Gly	Asp	Met	Ser	Arg	Lys	
65					70	_				75					80	
63	gtt		-+-	~~~	+=+	cat	+++	ana	tta	cct	agc	act	tta	gac	aac	288
agt	gtt	tta	gry	yaa	D	990	Dho	7	Ton	Pro	Sor	Ala	Len	Asp	Asn	
Ser	Val	Leu	val		Tyr	GIA	Pne	ALG	Dea	FIU	Ser	1110	200	95		
				85					90							226
cac	cct	tta	aaa	ttt	gat	gaa	ttt	atc	cat	aaa	aat	tgc	cag	LLC	CLL	336
Ara	Pro	Leu	Lvs	Phe	Asp	Glu	Phe	Ile	His	Lys	Asn	Cys	Gln	Phe	Leu	
my			100					105					110			
			100			+		cta	<b>722</b>	tta	σаσ	ctt	tec	aaa	ааσ	384
ttt	gtg	tcc	gct	acg	-	aat	aay	T	Gaa Gaa	Tan	67.	Tou	202	Tue	Lve	
Phe	Val	Ser	Ala	Thr	Pro	Asn	rys	rea	GIU	Leu	GIU	rea	Ser	Бyз	Буз	
		115					120					125				
aat	gtc	act	gag	caa	atc	att	cgc	cct	aca	ggg	ctt	tta	gac	cct	aaa	432
3	Val	712	Glu	Gla	Tle	Tle	Ara	Pro	Thr	Glv	Leu	Leu	Asp	Pro	Lys	
ASII			GIU	GIII	116		9			3	140		•		-	
	130					135								+		480
ttt	gaa	gtg	cga	gac	agc	gat	aag	caa	gtc	cag	gat	ttg	בננ	gat	gaa	400
Phe	Glu	Val	Arg	Asp	Ser	Asp	Lys	Gln	Val	Gln	Asp	Leu	Phe	Asp	Glu	
			•	•	150	•	-			155					160	
145	aag				444	200	an+	as s	-200		ctc	atc	acc	aco	ctc	528
atc	aag	tta	gtg	gra	gec	aya	990	900	299	y-9	Tan	Tlo	Thr.	Thr	Len	
Ile	Lys	Leu	Val	Val	Ala	Arg	GIA	GIU	Arg	val	ren	TIE	1111	1111	Leu	
	_			165					170					175		
	aaa	222	ato	gca	gaa	gaa	tta	tac	aaa	tat	tat	gct	gaa	tgg	ggc	576
act	Lys	T	Mat	214	61	6111	נים.ן	Cue	J.ve	Tvr	Tvr	Ala	Glu	Tro	Glv	
Thr	гys	τλg			GIU	GIU	Tea	105	2,3	-1-	- 1 -		190			
			180					185								60.4
tta	aag	gcq	cgt	tac	atg	cat	agt	gaa	att	gat	gcg	att	gaa	agg	aat	624
ים.ן	Lys	Ala	Ara	Tvr	Met	His	Ser	Glu	Ile	Asp	Ala	Ile	Glu	Arg	Asn	
neu		195		- ] **			200			-		205				
		1 7 3														
	atc	_ 4					a++	222	as s	+++	asc.	att	tta	ata	ggg	672

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	Ile 210					215					220					200
atc		ctt	tta	aga	gaa	ggg	ctg	gat	ttg	cct	gaa	gtc	tct	tta	gta	720
Tla	aat Asn	Len	Leu	Ara	Ğlu	Gly	Leu	Asp	Leu	Pro	Glu	Val	Ser	Leu		
005					つてい					233						
225	atc		ast	aca	~~+	aaa	gaa	qqq	ttt	tta	agg	agt	gaa	aca	agc	768
gcg	atc Ile	atg	gat	31-	Aco	T.ve	Glu	Glv	Phe	Leu	Arq	Ser	Glu	Thr	Ser	
Ala	IIe	Met	Asp	WIG	nsp	цуо		3	250					255		
				245				act	200	220	act	aat	aac		att	816
ctc	att	caa	acc	atg	ggg	cga	gcc	33-	200	Non-	λl-	yen	Clv	T.ve	Val	-
Leu	att Ile	Gln	Thr	Met	Gly	Arg	Ala	WIG	Arg	ASII	MIG	VOII	270	230	144	
			ってい					200					210			864
tta	tta	tac	gct	aaa	aag	atc	act	caa	agc	atg	caa	aaa	gcc	266	gag	004.
Leu	tta Leu	Tvr	Ala	Lys	Lys	Ile	Thr	Gln	Ser	Met	Gln	пуэ	Ala	Pne	GIU	
		275					280					203				010
atc	act		tac	agg	cgc	gcc	aaa	caa	gaa	gag	ttc	aat	aaa	atc	cat	912
Tlo	act Thr	Ser	Tvr	Arg	Ara	Ala	Lys	Gln	Glu	Glu	Phe	Asn	Lys	Ile	His	
	200					295					200					
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aac	atc Ile	acc	Dec	Tue	Th-	Vai	Thr	Ara	Ála	Leu	Ğlu	Glu	Glu	Leu	Lys	
		Thr	Pro	гуу	7117	Val	****	9		315					.320	
305			_		310		2+0	act	222		tta	aaa	ааσ	σac	aaa	1008
tta	aga	gac	gat	gaa	att	aga	Tin	71.	Tue	Mla	T.e.11	Lvs	Lvs	Asp	aaa Lvs	•
Leu	aga Arg	Asp	Asp	Glu	IIe	Arg	TTE	WIG	330	AIG	Deu	232	30	335	-3-	
				325			•						~~+		222	1056
atg	cct	aaa	agt	gaa	agg	gaa	aaa	atc	att	aaa	gaa	LLG	yac	Tuc	aaa Lvs	1050
Met	Pro	Lys	Ser	Glu	Arg	Glu	Lys	TTE	He	Lys	GIU	Leu	nap	гу	Lys	
			240					.345					330			1104
ato	сда	gaa	tqc	acg	aag	aat	ttg	gat	ttt	gaa	gaa	gcg	atg	cgt	ttg Len	1104
Met	Ara	Glu	Cvs	Thr	Lys	Asn	Leu	Asp	Phe	Glu	Glu	Ala	Met	Arg	Leu	
Nec		355			•		360					365				
	gac	722	atc	act	caa	tta	aga	acg	ctt							1134
aya	Asp	Glu	Tle	Δla	Gln	Leu	Arg	Thr	Leu							
Arg			110	n.u	· · · · ·	375										
-04	370															
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	13> H		obac	ter	БАто	ΙI										
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Glu	ı Tyr	Asn	Arg	Leu	гуs	GIII	ALY	1111	10				-	15		
1	L			5	_	•	<b>61</b>	T1.	Clu	) Nen	ጥረታ	. Ala	Arc			
Sei	c Ala	Thr	Gly	v Val	Cys	гÀг	GIÀ	116	GIU	, noi	. I y I	nio	30		Phe	
			20	١				23	1				20			
Thi	r Gly	, Lys	: Ala	Pro	Asn	Glu	Thr	Pro	rne	Cys	Leu	Pne	. Wat	, I Y I	Leu	
		20	•				40	1				4.5	,			
Gly	v Ile	.Phe	Glu	Arg	Glu	Phe	Leu	Val	Ile	Val	. Asp	GIU	Ser	HIS	Val	
						~~	١				U	,				
Sa	ים.	Pro	Glr	. Phe	Glv	Gly	Met	Tyr	Ala	Gly	/ Asp	Met	Ser	Arc	Lys 80	
	_				70	1				10	,					
6:	. 17-1		. 1/-1	Glu	ነ ጥህተ	Glv	Phe	Arc	Leu	Pro	Ser	Ala	Let	ı Asp	Asn	
				0 5					20	,					•	
	_	_		- Db-	, 	. c1.	Dhe	Tle	His	Lvs	Asr	Cvs	Glr	Phe	Leu	
Ar	g Pro	Let			, Ash	910	LINC	105				3 -	110	)		
			100	)		_	•	10-	, 		. 61.	. Lai			. I.vs	
Ph:	e Val	L Se	c Ala	a Thi	: Pro	) Asr	Lys	· rer	GIU	ı nec	GIU	100	: 561	. ду.	Lys	
		9 9 1	-				120	)				14.	,			
As		Ala	a Glu	ı Glr	ılle	: Ile	e Arg	Pro	Thr	GI	Let	ı Let	ı ASI	PIC	Lys	
	n Val					134	•				14/	,				
<b>5</b> 1		^							. 11-1	ഭിം	n Ast	ı I.eı	ı Phe	. Aqt	5 F2   31	
		^	l Ard	, Ast	Ser	Asr	Lys	Glr	rev	GII		, 200			, 614	
	130 e Gl	0 u Va			150	1				LJ.	,				100	
	130 e Gl	0 u Va			150	1				LJ.	,				100	
14 11	130 e Glo 5 e Ly:	0 u Va. s Lei	ı Va	l Val	150 L Ala	Arq	Gly	, Glu	170	Val	Lei	ı Ile	e Thi	Th:	r Leu 5	
14 11	130 e Glo 5 e Ly:	0 u Va. s Lei	ı Va	l Val	150 L Ala	Arq	Gly	, Glu	170	Val	Lei	ı Ile	e Thi	Th:	r Leu 5	
14 11	130 e Glo 5 e Ly:	0 u Va. s Lei	u Vai	l Val 165 t Ala	150 L Ala	Arq	Gly	Glu Cys	Arg 170 Lys	Val	Lei	ı Ile	Thi	Thi 179	Leu	
14 11	130 e Glo 5 e Ly:	0 u Va. s Lei	ı Va	l Val 165 t Ala	150 L Ala	Arq	Gly	, Glu	Arg 170 Lys	Val	Lei	ı Ile	e Thi	Thi 179	r Leu 5	

															_	
Leu	Lys		Arg	Tyr	Met	His	Ser	Glu	Ile	Asp	Ala	11e 205	Glu	Arg	Asn	
His	Ile	195 Ile	Arg	Ser	Leu	Arg	200 Leu	Lys	Glu	Phe	Asp 220		Leu	Ile	Gly	
<b>71</b> a	210 Asn	T	Tau	Ara	Glu	215 Glv	Leu	Asp	Leu	Pro	Glu	Val	Ser	Leu	Val	
	Aşn	Leu	Dea	Arg	230	,		•		235					240	•
225	Ile		_		230	7	G1 ₁₁	Glv	Dhe	I.eu	Ara	Ser	Glu	Thr	Ser	
Ala	Ile	Met	Asp	ALA	ASP	гуэ	Gra	OLY	250	200	,			255		
				245		•	21-	71-	250	N en	λla	a en	Glv		Val	
Leu	Ile	Gln	Thr	Met	GLA	Arg	Ala	Ald	ALG	MSII	VI.O	N3!!	270	-,-		
			260			_		265	_	L	C1 -	7		Dha	Glu	
	Leu	275					280					203				
	Thr 290	Ser				745					300					
<b>3</b>	230	mb ~	Dro	Lvs	Thr	Val	Thr	Ara	Ala	Leu	Glu	Glu	Glu	Leu	Lys	
	TTE	1111	110	בעם	310					315					320	
305	Arg	<b>-</b>	7	C1.,	Tla	Ara	Tle	Ala	Lvs	Ala	Leu	Lys	Lys	Asp	Lys	
				325					330					222		
Mot	Pro	I.vs	Ser	Glu	Arq	Glu	Lys	Ile	Ile	Lys	Glu	Leu	Asp	Lys	Lys	
			310					345					220			
Met	Arg	Glu 355	Cys	Thr	Lys	Asn	Leu 360	Asp	Phe	Glu	Glu	Ala 365	Met	Arg	Leu	
_	Asp	222	T1.	n1 a	Gln	T.e.u		Thr	Leu							
Arg	370	Gru	116	nia	02	375	5									
<21	0> 1	07														
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·21	3> H	olic	obac	ter	ovlo	ri										
		CTTC			-1											
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	1> C															
			1100	١												
			(498	)												
440	A- 1	Ω7			++>	222	act	tca	caa	σаа	ata	cag	gct	aac	acg	48
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ctt Lev gct Ala agt	0> 1 tcc Ser aag Lys aac Asn gaa Glu	tta Leu cag Gln cag Gln tta	cga Arg caa Gln 20 caa Gln ttg	gcc Ala 5 tcg Ser gct Ala acc	caa Gln atc Ile aag	Lys act Thr cag Gln tta	tta Leu cag Gln 40 ago	gag Glu 25 tta Leu cag Gln	gat Asp gac Asp gat Asp	ttg Leu aag Lys ttg	agg Arg caa Gln gtt 60 aaa	aat Asn aat Asn 45 tca Ser	gag Glu 30 aaa Lys caa Glr	15 att	cac His Atg Met GCC	96 144 192 240
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aaa Lys	gag Glu	agt Ser 35	aca	agt Ser	gaa Glu	atc Ile	gcg Ala 40	ctt Leu	aat Asn	tgg Trp	gct Ala	gaa Glu 45	gca Ala	gag Glu	ata Ile	144
aac Asn	Tyr	~>>	aat Asn	ttt Phe	aat Asn	aac Asn 55	gct Ala	aaa Lys	tac Tyr	ctc Leu	att Ile 60	gat Asp	aag Lys	gtg Val	gtc Val	192
Gln	50 tcc Ser	aac Asn	cct Pro	gat Asp	tat Tyr 70	att	tct Ser	acg Thr	cat His	agc Ser 75	gaa Glu	tca Ser	gcc Ala	cta Leu	gac Asp 80	240
65 ttg Leu	ctc Leu	aag Lys	tta Leu	ttg Leu	222	aaa Lys	aac Asn	cag Gln	atg Met 90	aat	gca Ala	agc Ser	gcg Ala	att Ile 95	gag Glu	288
atc Ile	gct Ala	cac His	Leu	85 ctc Leu	ctc Leu	aat Asn	caa Gln	gat Asp 105	gat	gat Asp	ctg Leu	aaa Lys	gct Ala 110	aaa Lys	gag Glu	336
caa Gln	gcg Ala	Leu	100 tat Tyr	gat Asp	tta Leu	gga Gly	gcg Ala 120	tta	tat Tyr	gca Ala	agg Arg	atc Ile 125	aag Lys	gac Asp	ttt Phe	384
aaa Lys	Asn	115 gcc Ala	cac His	ctt Leu	tac Tyr	aat Asn 135	cta	caa Gln	tat Tyr	ttg Leu	cag Gln 140	gac	cat His	gcg Ala	gaa Glu	432
ctg Leu	130 gat Asp	aaa Lys	gct Ala	tct Ser	Val	att	agg Arg	gcg Ala	cgc Arg	gat Asp 155	gaa	aaa Lys	gcc Ala	ctt Leu	ttt Phe 160	480
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att Ile	caa Gln	aat Asn	Phe	165 cct Pro	aat Asn	tct Ser	aat Asn	gaa Glu 185	qcc	cta	aag Lys	gct Ala	tta Leu 190	gaa Glu	ttg Leu	576
aaa Lys	gcc Ala	Gln	Leu	ttg Leu	ttt Phe	gaa Glu	Asn	aag Lys	cgt Arg	tat Tyr	gct Ala	gaa Glu 205	gtg Val	tta	agc Ser	624
atg Met	caa Gln	195 aaa Lys	22+	ttg Leu	cct Pro	Lys	Asp	tcc	cct Pro	ttg Leu	atc Ile 220	caa Gln	aaa	acg Thr	ctc Leu	672
aat Asn	210 gtc Val	-++	gct Ala	aaa Lys	Thr	215 cca Pro	tta	gag Glu	aac Asn	HIS	cgt Arg	tgt	gaa Glu	gaa Glu	gcc Ala 240	720
225 tta Leu		tat Tyr	tta Leu	tcc Ser	230 caa Gln	atc Ile	aca Thr	acc Thr	Phe	GIU	ttc	agc Ser	ccc Pro	пуэ	gaa Glu	768
			acc	245	gat	tac	tta	tat	ttc Phe	gca	tcg	ctc	aaa Lys	gaa Glu	aaa	816
		+.	260	400	cta	aac	act	265 ttt	aaa	acq	gct	aaa Lys	gcc	cct	agc Ser	864
		275					280					200	1		tta	912

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                                                                  932
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Lys Glu Ser Ala Ser Glu Ile Ala Leu Asn Trp Ala Glu Ala Glu Ile
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Asn Tyr Gln Asn Phe Asn Asn Ala Lys Tyr Leu Ile Asp Lys Val Val
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Gln Ser Asn Pro Asp Tyr Ile Ser Thr His Ser Glu Ser Ala Leu Asp
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Leu Leu Lys Leu Leu Lys Lys Asn Gln Met Asn Ala Ser Ala Ile Glu
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Ile Ala His Leu Leu Leu Asn Gln Asp Asp Asp Leu Lys Ala Lys Glu
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Gln Ala Leu Tyr Asp Leu Gly Ala Leu Tyr Ala Arg Ile Lys Asp Phe
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                            120
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Lys Asn Ala His Leu Tyr Asn Leu Gln Tyr Leu Gln Asp His Ala Glu
                                            140
                        135
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Leu Asp Lys Ala Ser Val Val Arg Ala Arg Asp Glu Lys Ala Leu Phe
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                    150
Ser Met Glu Gly Asn Thr Gln Glu Lys Ile Ala His Tyr Asp Lys Ile
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Ile Gln Asn Phe Pro Asn Ser Asn Glu Ala Leu Lys Ala Leu Glu Leu
                                                    190
            180
                                185
Lys Ala Gln Leu Leu Phe Glu Asn Lys Arg Tyr Ala Glu Val Leu Ser
                                                205
                            200
Met Gln Lys Asn Leu Pro Lys Asp Ser Pro Leu Ile Gln Lys Thr Leu
                                            220
                        215
Asn Val Leu Ala Lys Thr Pro Leu Glu Asn His Arg Cys Glu Glu Ala
                                        235
                   230
Leu Lys Tyr Leu Ser Gln Ile Thr Thr Phe Glu Phe Ser Pro Lys Glu
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                245
Glu Ile Gln Ala Phe Asp Cys Leu Tyr Phe Ala Ser Leu Lys Glu Lys
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            260
Ala Gln Ile Ile Ala Leu Asn Ala Phe Lys Thr Ala Lys Ala Pro Ser
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Glu Lys Leu Ile Trp Leu Tyr Arg Leu Gly Arg Asn Tyr Tyr Arg Leu
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		aat	20	tat	tct	tct	tta	25 caa	agc	σaa	cac	atc	30 aat	tcc	ccc	144
Ala	Asp	Asn 35	Tyr	Tyr	Ser	Ser	Leu 40	Gln	Ser	Ğlu	His	Ile 45	Asn	Ser	Pro	
ctt	atc	CCa	gaa	gcg	atg	cta	act	tta	ggg	caa	gcg	cac	atg	aaa	aag	192
Leu	Val	Pro	Glu	Ala	Met	Leu 55	Ala	Leu	GIŊ	GIN	60	HIS	met	гÃ2	Lys	2.42
aaa	gag	tat	gtt	tta	gcg	tct	ttt	tac	ttt	gat	gaa	tac	atc	aag	cgc Ara	240
66		Tyr			70					75					60	200
ttt	ggg	act	aag	gac	aat	gtg	gat	tat	ttg	act	Phe	Leu	Lvs	Leu	Gln	288
		Thr		85					90					73		336
tcg	cat	tat Tyr	tac	gct	Dhe	aaa Lvs	Asn	His	Ser	Lvs	Asp	Gln	Glu	Phe	Ile	
			100					105					110			204
tct	aat	tct	att	gtg	agt	tta	ggc	gaa	ttt	ata	gaa	aaa	Tur	Pro	Asn	384
		Ser 115					120					125				432
agc	cgt	tac Tyr	cgc	CCC	tat	gta	gaa.	Tur	Met	Gln	Ile	Lvs	Phe	Ile	Leu	172
	130					135					140				,	400
ggg	caa	aat	gag	ctc	aat	cgc	gcg	atc	gcg	aat	gtc	Tur	aaa Lvs	aaa I.vs	Ara	· 480
	Gln	Asn	Glu	Leu	Asn 150	Arg	ATS	TTE	AIA	155	Val	TAT	пуз	LyJ	160	
145	aan	cct	gag	aac	σtσ	aaa	cgc	tat	tta	qaa	agg	ata	gat	gag	act	528
His	Lys	Pro	Glu	Gly 165	Val	Lys	Arg	Tyr	Leu 170	GIU	Arg	ITE	Asp	175	IIIL	
tta	gaa	aaa	gag	act	aaa	ccc	aaa	сса	tcg	cac	atg	cct	tgg	tat	gtg	576
		Lys	180		Lys	Pro	Lys	Pro 185	Ser	HIS	Met	PIO	190	ıyı	Val	591
		ttt														391
		Phe 195	Asp	пр												
	0> 1 1> 1															
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		elic	obac	ter	Ьλτο	rı										
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Trp	Tyr	Gln		Ile	Leu	Arg	Glu	Ile 25	Leu	Phe	Ala	Asn	Leu 30	Glu	Thr	
Ala	Asp		20 Tyr	Tyr	Ser	Ser	Leu 40		Ser	Glu	His	Ile 45			Pro	
Leu			G1u	Ala	Met	Leu 55	Ala	Leu	Gly	Gln	Ala 60		Met	Lys	Lys	
		Tyr	Val	Leu	Ala 70	Ser	Phe	Tyr	Phe	Asp 75		Tyr	Ile	Lys	Arg 80	
65 Phe	Gly	Thr	Lys		Asn	Val	Asp	Tyr	Leu 90		Phe	Leu	Lys	Leu 95	Gln	
Ser	His	Tyr		85 Ala	Phe	Lys	Asn	His 105		Lys	Asp	Gln	Glu 110	Phe	Ile	
Ser	Asn			Val	Ser	Leu	Gly 120	Glu	Phe	Ile	Glu	Lys 125	Tyr		Asn	
Ser			Arg	Pro	Tyr	Val 135	Glu	Tyr	Met	Gln	Ile 140			Ile	Leu	
Glu	130 Gln	Asn	Glu	Leu	Asn	Arg	Ala	Ile	Ala	Asn		Tyr	Lys	Lys	Arg	
145					150	•				155					160	

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His Lys Pro Glu Gly Val Lys Arg Tyr Leu Glu Arg Ile Asp Glu Thr
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Leu Glu Lys Glu Thr Lys Pro Lys Pro Ser His Met Pro Trp Tyr Val
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Leu Ile Phe Asp Trp
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                                      10
                  5
caa aag tta ctg ata ggg gca gct aaa agc ggt tgc att caa tct agc
Gln Lys Leu Leu Ile Gly Ala Ala Lys Ser Gly Cys Ile Gln Ser Ser
             20
gct gat aaa ctg gct cag tta aaa acg cgc tta ctc tac tgg caa gac
Ala Asp Lys Leu Ala Gln Leu Lys Thr Arg Leu Leu Tyr Trp Gln Asp
                                                  45
                              40
         35
aaa tot gtt aaa gtg gat tgg gat aaa coc att tta atc aag gac tto
                                                                    192
Lys Ser Val Lys Val Asp Trp Asp Lys Pro Ile Leu Ile Lys Asp Phe
                         55
ttt aaa ggc aat aat tac ctt tat agg agg ttt tgt ttt tta ttg ggg
                                                                    240
Phe Lys Gly Asn Asn Tyr Leu Tyr Arg Arg Phe Cys Phe Leu Leu Gly
                                          75
. 65
aag cat ttt atg gac aga ttt tta aag aat aac gct aag gcg agc gtg
                                                                    288
Lys His Phe Met Asp Arg Phe Leu Lys Asn Asn Ala Lys Ala Ser Val
                                      90
                  85
aaa gac ttt atg tct agt aag gag ttt gtc gct aaa tac cga tac acc
                                                                    336
Lys Asp Phe Met Ser Ser Lys Glu Phe Val Ala Lys Tyr Arg Tyr Thr
                                                     110
                                 105
ccc aag caa aat aca gaa aga gcg aaa aag ctg caa tcg tat tta gag
                                                                    384
Pro Lys Gln Asn Thr Glu Arg Ala Lys Lys Leu Gln Ser Tyr Leu Glu
                                                 125
                             120
 aat aag cgc gat ttt ata ggg ttt gtt caa gcg ctt aac tct tta aaa
                                                                    432
Asn Lys Arg Asp Phe Ile Gly Phe Val Gln Ala Leu Asn Ser Leu Lys
                                             140
                         135
 gac aac ccg caa gat cct ttt tta ccc aat gaa gaa acg agc ttt ttg
                                                                    480
 Asp Asn Pro Gln Asp Pro Phe Leu Pro Asn Glu Glu Thr Ser Phe Leu
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                     150
                                                                    498
 gtg ttc gct aat gag cct
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 Ala Asp Lys Leu Ala Gln Leu Lys Thr Arg Leu Leu Tyr Trp Gln Asp
 Lys Ser Val Lys Val Asp Trp Asp Lys Pro Ile Leu Ile Lys Asp Phe
 Phe Lys Gly Asn Asn Tyr Leu Tyr Arg Arg Phe Cys Phe Leu Leu Gly
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75
Lys His Phe Met Asp Arg Phe Leu Lys Asn Asn Ala Lys Ala Ser Val
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Lys Asp Phe Met Ser Ser Lys Glu Phe Val Ala Lys Tyr Arg Tyr Thr
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                                105
            100
Pro Lys Gln Asn Thr Glu Arg Ala Lys Lys Leu Gln Ser Tyr Leu Glu
                            120
                                                125
Asn Lys Arg Asp Phe Ile Gly Phe Val Gln Ala Leu Asn Ser Leu Lys
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                        135
Asp Asn Pro Gln Asp Pro Phe Leu Pro Asn Glu Glu Thr Ser Phe Leu
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Val Phe Ala Asn Glu Pro
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Leu Ala Leu Asn Glu Leu Asn Pro Gly Glu Trp Val Val His Asp Asp
                                                          15
                  5
                                     10
tat ggg gtg ggc gtg ttt tct caa tta gtc cag cac agc gtt tta ggg
                                                                   96
Tyr Gly Val Gly Val Phe Ser Gln Leu Val Gln His Ser Val Leu Gly
                                 25
agc aag agg gat ttt tta gaa atc gct tat ttg ggc gaa gac aaa ctg
Ser Lys Arg Asp Phe Leu Glu Ile Ala Tyr Leu Gly Glu Asp Lys Leu
                             40
        35
ctg tta ccg gta gaa aac ttg cat ctc atc gct cgc tat gtg gcg caa
                                                                   192
Leu Leu Pro Val Glu Asn Leu His Leu Ile Ala Arg Tyr Val Ala Gln
                                           . 60
                         55
agc gat agc gtg cca gct aaa gac cgg cta ggg aaa ggg agc ttt ctt
                                                                    240
Ser Asp Ser Val Pro Ala Lys Asp Arg Leu Gly Lys Gly Ser Phe Leu
                     70
aaa tta aaa gct aaa gtc agg act aag ctt tta gag att gct agc aag
                                                                    288
Lys Leu Lys Ala Lys Val Arg Thr Lys Leu Leu Glu Ile Ala Ser Lys
                 85
atc att gaa tta gcg gct gaa cgc aat ttg atc ttg ggt aaa aag atg
                                                                    336
Ile Ile Glu Leu Ala Ala Glu Arg Asn Leu Ile Leu Gly Lys Lys Met
                                105
            100
gat gtg cat tta gcg gag ttg gaa gtc ttt aaa tcg cat gcg ggg ttt
                                                                    384
Asp Val His Leu Ala Glu Leu Glu Val Phe Lys Ser His Ala Gly Phe
                                                 125
                             120
                                                                    399
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Glu Tyr Thr Ser Asp
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Tyr Gly Val Gly Val Phe Ser Gln Leu Val Gln His Ser Val Leu Gly
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Ser Lys Arg Asp Phe Leu Glu Ile Ala Tyr Leu Gly Glu Asp Lys Leu
                             40
Leu Leu Pro Val Glu Asn Leu His Leu Ile Ala Arg Tyr Val Ala Gln
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60

55

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Ser Asp Ser Val Pro Ala Lys Asp Arg Leu Gly Lys Gly Ser Phe Leu
                     70
Lys Leu Lys Ala Lys Val Arg Thr Lys Leu Leu Glu Ile Ala Ser Lys
                                     90
                 85
Ile Ile Glu Leu Ala Ala Glu Arg Asn Leu Ile Leu Gly Lys Lys Met
                                                    110
                                105
Asp Val His Leu Ala Glu Leu Glu Val Phe Lys Ser His Ala Gly Phe
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Glu Tyr Thr Ser Asp
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Val Leu Asn Ala Pro Ile Thr Leu Glu Asp Ile Gln Glu Leu Ser Ser
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aat gcg ggg gat atg gat ttg caa aag ctc att tta ggg ctt ttt tta
                                                                   96
Asn Ala Gly Asp Met Asp Leu Gln Lys Leu Ile Leu Gly Leu Phe Leu
                                 25
             20
aaa aaa agt gcg ctt gat att tat gat tat ttg tta aaa gag ggc aaa
Lys Lys Ser Ala Leu Asp Ile Tyr Asp Tyr Leu Leu Lys Glu Gly Lys
                             40
                                                 45
         35
aaa gat gcg gat att tta agg ggg tta gag cgc tat ttt tac caa ctt
                                                                   192
Lys Asp Ala Asp Ile Leu Arg Gly Leu Glu Arg Tyr Phe Tyr Gln Leu
                                              60
                         55
ttt tta ttt ttc gct cat att aaa acg acc ggt tta atg gac gct aaa
                                                                   240
Phe Leu Phe Phe Ala His Ile Lys Thr Thr Gly Leu Met Asp Ala Lys
                     70
                                         75
 65
gag gtt tta ggc tac gct ccc cct aaa gaa att gcc gaa aat tac gct
                                                                   288
Glu Val Leu Gly Tyr Ala Pro Pro Lys Glu Ile Ala Glu Asn Tyr Ala
                                     90
                 85
                                                                   336
aaa aac gcc ttg cgt ttg aaa gaa gcc ggc tat aag agg gtt ttt gaa
Lys Asn Ala Leu Arg Leu Lys Glu Ala Gly Tyr Lys Arg Val Phe Glu
                                105
                                                     110
            100
att ttt agg tta tgg cac att caa agc atg caa ggg caa aag gaa ttg
                                                                   384
Ile Phe Arg Leu Trp His Ile Gln Ser Met Gln Gly Gln Lys Glu Leu
                            120
                                                 125
       115
ggc ttt ttg tat ttg acc tcc att caa aaa atc att aac ccc
                                                                   426
Gly Phe Leu Tyr Leu Thr Ser Ile Gln Lys Ile Ile Asn Pro
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                        135
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                                 25
Lys Lys Ser Ala Leu Asp Ile Tyr Asp Tyr Leu Leu Lys Glu Gly Lys
                             40
Lys Asp Ala Asp Ile Leu Arg Gly Leu Glu Arg Tyr Phe Tyr Gln Leu
                         55
Phe Leu Phe Phe Ala His Ile Lys Thr Thr Gly Leu Met Asp Ala Lys
                     70
Glu Val Leu Gly Tyr Ala Pro Pro Lys Glu Ile Ala Glu Asn Tyr Ala
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90
                85
Lys Asn Ala Leu Arg Leu Lys Glu Ala Gly Tyr Lys Arg Val Phe Glu
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           100
Ile Phe Arg Leu Trp His Ile Gln Ser Met Gln Gly Gln Lys Glu Leu
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       115
Gly Phe Leu Tyr Leu Thr Ser Ile Gln Lys Ile Ile Asn Pro
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Glu Glu Cys Gly Thr Leu Leu Glu Leu Arg Glu Lys Ile Ser Leu Phe
                 5
tta gag cca aag gat att gtt aaa act tat gaa aat gaa gat ttt aaa
                                                                 96
Leu Glu Pro Lys Asp Ile Val Lys Thr Tyr Glu Asn Glu Asp Phe Lys
                                25
             20
gag cgt tgt tta gcg ctt ttt aac gct cta aca agc atg gat ttt caa
                                                                 144
Glu Arg Cys Leu Ala Leu Phe Asn Ala Leu Thr Ser Met Asp Phe Gln
                                                45
                             40
         35
Ala Tyr Lys Asp Phe Glu Ser Phe Lys Lys Glu Ala Met Arg Leu Ser
                                            60
                         55
cag ctt aag ggt aag gat ttt ttc aaa cct ttg cgc atc ctt tta acc
                                                                 240
Gln Leu Lys Gly Lys Asp Phe Phe Lys Pro Leu Arg Ile Leu Leu Thr
                                        75
                     70
 65
ggg aac tcg cat ggc gtt gaa ttg cct ttg att ttc ccc tat atc caa
                                                                 288
Gly Asn Ser His Gly Val Glu Leu Pro Leu Ile Phe Pro Tyr Ile Gln
                 85
                                                                 297
agc cat cat
Ser His His
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 Glu Arg Cys Leu Ala Leu Phe Asn Ala Leu Thr Ser Met Asp Phe Gln
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 Ala Tyr Lys Asp Phe Glu Ser Phe Lys Lys Glu Ala Met Arg Leu Ser
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 Gln Leu Lys Gly Lys Asp Phe Phe Lys Pro Leu Arg Ile Leu Leu Thr
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 Ser His His
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Pro Gln Ile Val Ala Lys Asp Phe Leu Glu Arg Leu Gly Leu
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                                                                   84
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Ser His Lys Met Ala Lys Asp Leu Leu Gly Ile Ser
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Ser His Lys Met Ala Lys Asp Leu Leu Gly Ile Ser
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His Ile Tyr Glu Lys Glu Val Asp Ala Arg Glu Leu Lys His Gly Val
                                     10
gaa gaa ttt acc gct gat att cct gat gtg aaa gaa gaa gcg ctc gct
                                                                   96
Glu Glu Phe Thr Ala Asp Ile Pro Asp Val Lys Glu Glu Ala Leu Ala
cat ctt gat gaa agc ggg atc gtt aaa gtc ggt act tat gtg agc gct
                                                                   144
His Leu Asp Glu Ser Gly Ile Val Lys Val Gly Thr Tyr Val Ser Ala
                             40
         35
ggc atg att ttg gtg ggc aaa act tct cct aaa ggc gag att aaa agc
                                                                   192
Gly Met Ile Leu Val Gly Lys Thr Ser Pro Lys Gly Glu Ile Lys Ser
acg cct gaa gag cgg ctt tta agg gct att ttt ggg gat aaa gcc ggg
                                                                   240
Thr Pro Glu Glu Arg Leu Leu Arg Ala Ile Phe Gly Asp Lys Ala Gly
                     70
cat gtg gtc aat aag agt ttg tat tgc cct ccc agt ttg gaa ggc acg
                                                                   288
His Val Val Asn Lys Ser Leu Tyr Cys Pro Pro Ser Leu Glu Gly Thr
                                      90
gtg att gat gtg aaa gtc ttc act aaa aaa ggc tat gag aaa gac gcg
                                                                   336
Val Ile Asp Val Lys Val Phe Thr Lys Lys Gly Tyr Glu Lys Asp Ala
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110
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            100
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Arg Val Leu Ser Ala Tyr
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Glu Glu Phe Thr Ala Asp Ile Pro Asp Val Lys Glu Glu Ala Leu Ala
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His Leu Asp Glu Ser Gly Ile Val Lys Val Gly Thr Tyr Val Ser Ala
                             40
Gly Met Ile Leu Val Gly Lys Thr Ser Pro Lys Gly Glu Ile Lys Ser
                         55
Thr Pro Glu Glu Arg Leu Leu Arg Ala Ile Phe Gly Asp Lys Ala Gly
                                          75
                     70
His Val Val Asn Lys Ser Leu Tyr Cys Pro Pro Ser Leu Glu Gly Thr
                                      90
                 85
Val Ile Asp Val Lys Val Phe Thr Lys Lys Gly Tyr Glu Lys Asp Ala
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Arg Val Leu Ser Ala Tyr
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 Tyr Lys Pro Tyr Thr Pro Ser Arg Arg Phe Met Ser Val Leu Asp Ser
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 aaa gac att acc gca aaa agc agt gtc aaa ggc tta ctc act aag ctt
  1
Lys Asp Ile Thr Ala Lys Ser Ser Val Lys Gly Leu Leu Thr Lys Leu
                                  25
              20
 aaa gca aca gca ggg aga aac aat aac ggg cgc atc acc agc cgc cac
                                                                    144
 Lys Ala Thr Ala Gly Arg Asn Asn Gly Arg Ile Thr Ser Arg His
                              40
          35
 aaa gag aga ggg gct aaa aaa ctc tat cgc att att gat ttc aag cgc
                                                                    192
 Lys Glu Arg Gly Ala Lys Lys Leu Tyr Arg Ile Ile Asp Phe Lys Arg
                                              60
                          55
 aat aaa tac aat att gaa ggg aaa gtg gct gcg att gag tat gat cct
                                                                    240
 Asn Lys Tyr Asn Ile Glu Gly Lys Val Ala Ala Ile Glu Tyr Asp Pro
                                          75
                      70
 tac aga aat gcg cgc atc gct ctt gta gtc tat cct gat ggg gac aaa
                                                                    288
 Tyr Arg Asn Ala Arg Ile Ala Leu Val Val Tyr Pro Asp Gly Asp Lys
                                      90
                  85
 cgc tat att tta cag cca agc ggt ttg aaa gtg ggc gat agc gtt atc
 Arg Tyr Ile Leu Gln Pro Ser Gly Leu Lys Val Gly Asp Ser Val Ile
                                 105
             100
 gct gct gaa ggc ggt ttg gat att aaa gtg ggc ttt gcg atg aag tta
                                                                    384
 Ala Ala Glu Gly Gly Leu Asp Ile Lys Val Gly Phe Ala Met Lys Leu
                             120
 aaa aat atc ccc ata gga acg gtg gtg cat aat att gaa atg cat cca
                                                                    432
 Lys Asn Ile Pro Ile Gly Thr Val Val His Asn Ile Glu Met His Pro
                         135
     130
 ggg gct ggc ggg caa tta gcc aga agc gca gga atg agc gct caa atc
                                                                    480
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Gly Ala Gly Gly Gln Leu Ala Arg Ser Ala Gly Met Ser Ala Gln Ile
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                    150
atg ggt aga gaa aat aaa tac acc att att agg atg cca agc tct gaa
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Met Gly Arg Glu Asn Lys Tyr Thr Ile Ile Arg Met Pro Ser Ser Glu
                165
                                    170
atg cgc tac att cta agc gaa tgt atg gcg agt gtt ggc gtg gta ggg
                                                                   576
Met Arg Tyr Ile Leu Ser Glu Cys Met Ala Ser Val Gly Val Val Gly
                                185
                                                    190
            180
aat gag gat ttt atc aat gtc tct atc ggt aag gca ggg cgt aac cgc
                                                                   624
Asn Glu Asp Phe Ile Asn Val Ser Ile Gly Lys Ala Gly Arg Asn Arg
                                                205
                            200
        195
cac aga ggg atc cgc cca caa act cgt ggt agc gcg atg aac cca gtg
                                                                   672
His Arg Gly Ile Arg Pro Gln Thr Arg Gly Ser Ala Met Asn Pro Val
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gat cac ccg cat ggt ggg ggt gag gg
                                                                   698
Asp His Pro His Gly Gly Glu
225
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Tyr Lys Pro Tyr Thr Pro Ser Arg Arg Phe Met Ser Val Leu Asp Ser
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Lys Asp Ile Thr Ala Lys Ser Ser Val Lys Gly Leu Leu Thr Lys Leu
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Lys Ala Thr Ala Gly Arg Asn Asn Gly Arg Ile Thr Ser Arg His
         35
Lys Glu Arg Gly Ala Lys Lys Leu Tyr Arg Ile Ile Asp Phe Lys Arg
                         55
Asn Lys Tyr Asn Ile Glu Gly Lys Val Ala Ala Ile Glu Tyr Asp Pro
                     70
                                         75
Tyr Arg Asn Ala Arg Ile Ala Leu Val Val Tyr Pro Asp Gly Asp Lys
                                     90
                 85
Arg Tyr Ile Leu Gln Pro Ser Gly Leu Lys Val Gly Asp Ser Val Ile
                                105
            100
Ala Ala Glu Gly Gly Leu Asp Ile Lys Val Gly Phe Ala Met Lys Leu
                            120
                                                125
Lys Asn Ile Pro Ile Gly Thr Val Val His Asn Ile Glu Met His Pro
                        135
                                            140
Gly Ala Gly Gly Gln Leu Ala Arg Ser Ala Gly Met Ser Ala Gln Ile
                                        155
                    150
Met Gly Arg Glu Asn Lys Tyr Thr Ile Ile Arg Met Pro Ser Ser Glu
                                                        175
                165
                                    170
Met Arg Tyr Ile Leu Ser Glu Cys Met Ala Ser Val Gly Val Val Gly
                                185
            180
Asn Glu Asp Phe Ile Asn Val Ser Ile Gly Lys Ala Gly Arg Asn Arg
                                                205
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                            200
His Arg Gly Ile Arg Pro Gln Thr Arg Gly Ser Ala Met Asn Pro Val
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Asp His Pro His Gly Gly Glu
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225
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Tyr Asp Trp Ile Lys Glu Phe Val Arg Asp Gln Gly Glu Phe Ile Ala
                                     10
caa caa agc ggg tgg ctg gaa tta gag cga tca agc tat gcc aaa ctc
Gln Gln Ser Gly Trp Leu Glu Leu Glu Arg Ser Ser Tyr Ala Lys Leu
                                 25
atc gcg caa acc atc tcg cat gtg ctt aat ggc gga tcg ctg ttg gtg
Ile Ala Gln Thr Ile Ser His Val Leu Asn Gly Gly Ser Leu Leu Val
                             40
age geg gat tet tet agg cae tgg ttt tta aac tae att ett tet aac
Ser Ala Asp Ser Ser Arg His Trp Phe Leu Asn Tyr Ile Leu Ser Asn
                                             60
                         55
cta aac ccc aaa gat tta aaa gag cgc ccc tta ttg tcc gtc att gat
Leu Asn Pro Lys Asp Leu Lys Glu Arg Pro Leu Leu Ser Val Ile Asp
                                         75
                     70
ttt aac gct tct tct ttc tac ccc aaa aac gat gcg aat ctc tct cta
                                                                   288
Phe Asn Ala Ser Ser Phe Tyr Pro Lys Asn Asp Ala Asn Leu Ser Leu
                 85
gcc acc ata gag atg act tat caa aac ccc atg ttt tgg cat gtt ggg
                                                                   336
Ala Thr Ile Glu Met Thr Tyr Gln Asn Pro Met Phe Trp His Val Gly
                                105
            100
aaa att gaa aat gaa ggc tta aaa acg ata cta ttg agt aaa atc cct
Lys Ile Glu Asn Glu Gly Leu Lys Thr Ile Leu Leu Ser Lys Ile Pro
                                                125
                            120
agt ttt tta tgg ctt ttt gaa gag ctt aaa gaa gat tgc ttg ctt tta
                                                                   432
Ser Phe Leu Trp Leu Phe Glu Glu Leu Lys Glu Asp Cys Leu Leu
                        135
aaa gag cat gac agc ttg ctg gat tat aaa tta ttg cag ctc ttc aaa
                                                                   480
Lys Glu His Asp Ser Leu Leu Asp Tyr Lys Leu Leu Gln Leu Phe Lys
                    150
                                        155
ctc ttt gaa aac gcg ctt ttt agc gtg cta tac aat aag gtt act ctg
                                                                   528
Leu Phe Glu Asn Ala Leu Phe Ser Val Leu Tyr Asn Lys Val Thr Leu
                165
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<211> 176
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Tyr Asp Trp Ile Lys Glu Phe Val Arg Asp Gln Gly Glu Phe Ile Ala
Gln Gln Ser Gly Trp Leu Glu Leu Glu Arg Ser Ser Tyr Ala Lys Leu
Ile Ala Gln Thr Ile Ser His Val Leu Asn Gly Gly Ser Leu Leu Val
                             40
Ser Ala Asp Ser Ser Arg His Trp Phe Leu Asn Tyr Ile Leu Ser Asn
Leu Asn Pro Lys Asp Leu Lys Glu Arg Pro Leu Leu Ser Val Ile Asp
                                         75
Phe Asn Ala Ser Ser Phe Tyr Pro Lys Asn Asp Ala Asn Leu Ser Leu
                                     90
Ala Thr Ile Glu Met Thr Tyr Gln Asn Pro Met Phe Trp His Val Gly
                                105
Lys Ile Glu Asn Glu Gly Leu Lys Thr Ile Leu Leu Ser Lys Ile Pro
                            120
                                                125
Ser Phe Leu Trp Leu Phe Glu Glu Leu Lys Glu Asp Cys Leu Leu Leu
                                            140
                        135
Lys Glu His Asp Ser Leu Leu Asp Tyr Lys Leu Leu Gln Leu Phe Lys
                                        155
                    150
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<211> 263

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                                      10
                  5
aat tac ttt agc caa ctc aaa tac aac cct aac gca agc aag agc gat
                                                                   96
Asn Tyr Phe Ser Gln Leu Lys Tyr Asn Pro Asn Ala Ser Lys Ser Asp
                                 25
             20
att gcc ttt ttt tat gcc ccc aac caa gtc tta tgc acc acg att aca
                                                                   144
Ile Ala Phe Phe Tyr Ala Pro Asn Gln Val Leu Cys Thr Thr Ile Thr
                              40
         35
gct aaa tac ggc gcg ttg ctt aaa gaa att tta agc cag aat aaa gtc
                                                                   192
Ala Lys Tyr Gly Ala Leu Leu Lys Glu Ile Leu Ser Gln Asn Lys Val
                         55
ggc atg cat tta gcc cac agc gtg gat gtg cgt att gaa gta gcg cct
                                                                   240
Gly Met His Leu Ala His Ser Val Asp Val Arg Ile Glu Val Ala Pro
                                          75
                     70
 65
                                                                    263
aaa atc caa att aac gcc caa tc
Lys Ile Gln Ile Asn Ala Gln
                 85
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<211> 87
<212> PRT
<213> Helicobacter pylori
<400> 134
Leu Ala Leu Val Lys Gln Asn Pro Lys Val Ser Leu Ile Glu Tyr Glu
                                      10
  1
Asn Tyr Phe Ser Gln Leu Lys Tyr Asn Pro Asn Ala Ser Lys Ser Asp
                                  25
             20
Ile Ala Phe Phe Tyr Ala Pro Asn Gln Val Leu Cys Thr Thr Ile Thr
                              40
Ala Lys Tyr Gly Ala Leu Leu Lys Glu Ile Leu Ser Gln Asn Lys Val
                         55
     50
Gly Met His Leu Ala His Ser Val Asp Val Arg Ile Glu Val Ala Pro
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Lys Ile Gln Ile Asn Ala Gln
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<213> Helicobacter pylori
<220>
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ago tat goo aaa oto ato gog caa aco ato tog cat gtg ott aat ggo
                                                                    48
Ser Tyr Ala Lys Leu Ile Ala Gln Thr Ile Ser His Val Leu Asn Gly
                                      10
gga tcg ctg ttg gtg agc gcg gat tct tct agg cac tgg ttt tta aac
                                                                    96
Gly Ser Leu Leu Val Ser Ala Asp Ser Ser Arg His Trp Phe Leu Asn
                                  25
tac att ctt tct aac cta aac ccc aaa gat tta aaa gag cgc ccc tta
Tyr Ile Leu Ser Asn Leu Asn Pro Lys Asp Leu Lys Glu Arg Pro Leu
                                                  45
                              40
ttg tcc gtc att gat ttt aac gct tct tct ttc tac ccc aaa aac gat
Leu Ser Val Ile Asp Phe Asn Ala Ser Ser Phe Tyr Pro Lys Asn Asp
                          55
      50
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gcg aat ctc tct cta gcc acc ata gag atg act tat caa aac ccc atg
                                                                   240
Ala Asn Leu Ser Leu Ala Thr Ile Glu Met Thr Tyr Gln Asn Pro Met
ttt tgg cat gtt ggg aaa att gaa aat gaa ggc tta aaa acg ata cta
                                                                   288
Phe Trp His Val Gly Lys Ile Glu Asn Glu Gly Leu Lys Thr Ile Leu
ttg agt aaa atc cct agt ttt tta tgg ctt ttt gaa gag ctt aaa gaa
                                                                   336
Leu Ser Lys Ile Pro Ser Phe Leu Trp Leu Phe Glu Glu Leu Lys Glu
                                105
gat tgc ttg ctt tta aaa gag cat gac agc ttg ctg gat tat aaa tta
                                                                   384
Asp Cys Leu Leu Leu Lys Glu His Asp Ser Leu Leu Asp Tyr Lys Leu
                            120
        115
ttg cag ctc ttc aaa ctc ttt gaa aac gcg ctt ttt agc gtg cta tac
                                                                   432
Leu Gln Leu Phe Lys Leu Phe Glu Asn Ala Leu Phe Ser Val Leu Tyr
                        135
                                                                   447
aat aag gtt act ctg
Asn Lys Val Thr Leu
145
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<213> Helicobacter pylori
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Ser Tyr Ala Lys Leu Ile Ala Gln Thr Ile Ser His Val Leu Asn Gly
Gly Ser Leu Leu Val Ser Ala Asp Ser Ser Arg His Trp Phe Leu Asn
Tyr Ile Leu Ser Asn Leu Asn Pro Lys Asp Leu Lys Glu Arg Pro Leu
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Leu Ser Val Ile Asp Phe Asn Ala Ser Ser Phe Tyr Pro Lys Asn Asp
Ala Asn Leu Ser Leu Ala Thr Ile Glu Met Thr Tyr Gln Asn Pro Met
                     70
Phe Trp His Val Gly Lys Ile Glu Asn Glu Gly Leu Lys Thr Ile Leu
                 85
Leu Ser Lys Ile Pro Ser Phe Leu Trp Leu Phe Glu Glu Leu Lys Glu
                                105
           100
Asp Cys Leu Leu Lys Glu His Asp Ser Leu Leu Asp Tyr Lys Leu
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                                                125
Leu Gln Leu Phe Lys Leu Phe Glu Asn Ala Leu Phe Ser Val Leu Tyr
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Asn Lys Val Thr Leu
145
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atc gca aaa gaa gtg gga gcg ctc acg att gct atc gtt acc aag cct
Ile Ala Lys Glu Val Gly Ala Leu Thr Ile Ala Ile Val Thr Lys Pro
ttc aaa tac gaa ggg aat caa aaa aga aag agg gct gaa gag gga ttg
Phe Lys Tyr Glu Gly Asn Gln Lys Arg Lys Arg Ala Glu Glu Gly Leu
                             40
aaa gaa ttg gag cag tct agc gat tct att ttg gtt atc cct aat gac
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Lys	50					55					60					
222	atc	ctt	ctc	acc	atq	aaa	aaa	aac	gct	agc	acc	acg	gag	tgt	tat	240
Lys	Tle	Len	Leu	Thr	Met	Lvs	Lys	Asn	Ala	Ser	Thr	Thr	Glu	Cys	Tyr	
65	110	204			70		•			75					80	
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agg	gaa	gul	gat	Asp	ycc val	Lou	Val	Ara	Ala	Val	Ser	Glv	Tle	Ser	Thr	
Arg	GIU	var	Asp		Val	Dea	Val	мy	90	141	001	1		95		
				85								~~~	ast		220	336
atc	atc	act	aaa	CCC	ggt	aat	atc	aat	get	yat	Db.	310	yar Nan	LCa	Tue	330
Ile	Ile	Thr	Lys	Pro	Gly	Asn	IIe	Asn	vaı	Asp	Pne	ATG	Asp	rea	гåа	
			100					105					110			
aqc	gct	ctt	ggt	ttt	aaa	ggc	ttt	gcg	tta	atg	ggt	att	ggt	gaa	gcc	384
Ser	Ala	Leu	Gly	Phe	Lys	Gly	Phe	Ala	Leu	Met	Gly	Ile	Gly	Glu	Ala	
		115					120					125				
act	aac	gaa	gaa	tcc	gct	aaa	tta	gcg	gtg	caa	aat	gcg	atc	caa	tcg	432
Thr	Glv	Glu	Ğlu	Ser	Āla	Lys	Leu	Ala	Val	Gln	Asn	Ala	Ile	Gln	Ser	
1111	130					135					140					
+	250	ctt	nat.	gac	act	tct	att	σaa	aaa	qct	aag	agc	att	att	gtc	480
Doo	Ton	Lou	Den	Asp	Ala	Ser	Ile	Glu	Gĺv	Ála	Lvs	Ser	Ile	Ile	Val	
	Leu	Leu	vaħ	wah	150				,	155	-3-				160	
145				cac	224	ast	tat	cct	ata		act	tat	tct	caa	aca	528
ttt	ttt	gag	cac	His	Door	yat	T	Dro	Mat	Mot	Mla	Tur	Ser	Gln	Ala	
Phe	Phe	GIu	HIS		Pro	Asp	ıyı	PIO	170	ine c	VIG	- 7 -	001	175		
				165					170			~~~	~++		+++	576
tgc	gat	ttt	att	caa	gat	caa	gcc	cat	caa	gat	guu	yac	yct Wal	aay T	Pho	. 310
Cys	Asp	Phe	Ile	Gln	Asp	Gln	Ala	His	GIn	Asp	vai	Asp	val	гая	Pile	
			180					185					190			<b>CO</b> 4
qqc	caa	cac	acg	agc	gat	aat	atc	cct	att	gat	cat	gtg	cgc	gtt	act	624
Ğĺv	Gln	His	Thr	Ser	Asp	Asn	Ile	Pro	Ile	Asp	His	Val	Arg	Val	Thr	•
_		195					200					205				4-4
atc	att	qca	acc	ggt	gct	gaa	aga	aac	agc	ggt	gga	gcg	agt	ttg	gaa	672
Tle	Ile	Ála	Thr	Gly	Ala	Glu	Arg	Asn	Ser	Gly	Gly	Ala	Ser	Leu	Glu	
	210					215					220					
tct	atc	act	acq	ccc	tct	caq	cct	gtg	gtg	aaa	caa	acg	aga	aaa	gtg	720
Car	Tla	Δla	Thr	Pro	Ser	Gln	Pro	Val	Val	Lys	Gln	Thr	Arg	Lys	Val	
225	110			,	230					235					240	
	t	aac	aaa	tat	tta	aag	atc	cct	act	qaa	gaa	gag	cta	tcc	ata	768
990	Aac Aan	Glv	Glu	Tyr	Leu	Lvs	Ile	Pro	Thr	Ğlu	Ğlu	Glu	Leu	Ser	Ile	
GTA	ASII	Gry	GIU	245	200	_,_			250					255		
			~+ <i>~</i>	aga	ato	can	caa	gac					•			795
CCC	aca	acc	Mat	Arg	Tio	Cln	Cla	Asn								
Pro	Thr	Int		ALY	116	0111	<b>U</b> I	265								
			260					203								
	0> 1															
	1> 2															
	2> P															
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Gly	Leu	Gly	Gly	Gly	Thr	GTĀ	Thr	GTĀ	ALA	Thr	Pro	Thr	TTE	Val	Lys	
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Ile	Ala	Lys	Glu	Val	Gly	Ala	Leu	Thr	Ile	Ala	Ile	Val	Thr	ьys	Pro	
			20					25					30			
Phe	Lvs	Tvr	Glu	Gly	Asn	Gln	Lys	Arg	Lys	Arg	Ala	Glu	Glu	Gly	Leu	
	-1-	35		•	•		40					45				
T	G1 ₁₁	1.011	Glu	Gln	Ser	Ser	Asp	Ser	Ile	Leu	Val	Ile	Pro	Asn	Asp	
гÀэ			014	Ų	-	55					60					
	50	1	T 0	mb.~	Mot		T.ve	Asn	Ala	Ser	Thr	Thr	Glu	Cvs	Tyr	
		ren	neg	IIII		nya	nya			75				- ] -	80	
65					70	<b>T</b> =	17- 7	N	<b>71</b> -		60-	G1 · ·	710	Ser		•
Arg	Glu	Val	Asp			ren	vaı	MIG	WIG	AGT	361	GTÅ	116	OET	Thr	
٠				85		_		_	90	_	<b>5</b> 1			95		
Ile	Ile	Thr	Lys	Pro	Gly	Asn	Ile	Asn	val	Asp	rne	ATA	ASP	ьeu	Lys	
			100					105					110			
Ser	Ala	Leu	Gly	Phe	Lys	Gly	Phe	Ala	Leu	Met	Gly	Ile	Gly	GLu	Ala	
			-													

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120
        115
Thr Gly Glu Glu Ser Ala Lys Leu Ala Val Gln Asn Ala Ile Gln Ser
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Pro Leu Leu Asp Asp Ala Ser Ile Glu Gly Ala Lys Ser Ile Ile Val
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                    150
Phe Phe Glu His His Pro Asp Tyr Pro Met Met Ala Tyr Ser Gln Ala
                                     170
                165
Cys Asp Phe Ile Gln Asp Gln Ala His Gln Asp Val Asp Val Lys Phe
                                                     190
                                185
            180
Gly Gln His Thr Ser Asp Asn Ile Pro Ile Asp His Val Arg Val Thr
                                                 205
                            200
        195
Ile Ile Ala Thr Gly Ala Glu Arg Asn Ser Gly Gly Ala Ser Leu Glu
                                             220
                        215
    210
Ser Ile Ala Thr Pro Ser Gln Pro Val Val Lys Gln Thr Arg Lys Val
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gcg ttt caa aaa agc act caa gct aaa atc gtt caa gtg tgt ggt ttt
                                                                    96
Ala Phe Gln Lys Ser Thr Gln Ala Lys Ile Val Gln Val Cys Gly Phe
                                                      30
                                 25
             20
aac ccc cat gcg ggc gaa gag ggc tta ttt ggg gaa gaa gat gaa agg
Asn Pro His Ala Gly Glu Glu Gly Leu Phe Gly Glu Glu Asp Glu Arg
                             40
att tta aaa gcc att caa aag agc aac caa acg cta ggc ttt gaa tgc
                                                                    192
Ile Leu Lys Ala Ile Gln Lys Ser Asn Gln Thr Leu Gly Phe Glu Cys
                          55
                                              60
 ttt ttg ggg cca ctg ccg gct gat agt gct ttt gcc ccc aat aaa cga
                                                                    240
 Phe Leu Gly Pro Leu Pro Ala Asp Ser Ala Phe Ala Pro Asn Lys Arg
                      70
 aaa ata acc cct ttt tat gtg agc atg agc cat gat gtg ggg cta gcc
                                                                    288
 Lys Ile Thr Pro Phe Tyr Val Ser Met Ser His Asp Val Gly Leu Ala
                  85
 cct tta aaa gcg ctc tat ttt gat gaa agc att aat gtg agt ttg aac
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 Pro Leu Lys Ala Leu Tyr Phe Asp Glu Ser Ile Asn Val Ser Leu Asn
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 gcc ccc
 Ala Pro
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 Asn Pro His Ala Gly Glu Glu Gly Leu Phe Gly Glu Glu Asp Glu Arg
                              40
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65	Leu	_			70				Ala	75					80	
Lys	Ile	Thr	Pro	Phe 85	Tyr	Val	Ser	Met	Ser 90	His	Asp	Val	Gly	Leu 95	Ala	
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Ala	Pro															
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Ile	Val	cat His	Pro	att Ile	Cys	Val 55	Ala	Ser	Leu	vaı	60 ATA	Pne	Cys	GTĀ	GIĀ	192
Asp 65	gag Glu	Ala	Met	gtg Val	Cys 70	Ala	Ala	Leu	Leu	His 75	Asp	vaı	Vai	GIU	Asp 80	240
açg Thr	Pro	Cys	Lys	att Ile 85	Glu	Thr	Ile	Glu	Gln 90	Glu	Phe	GTÀ	GIN	Asp 95	vai	288
gct Ala	aat Asn	tta Leu	gtg Val 100	gat Asp	gcg Ala	ctc Leu	act Thr	aaa Lys 105	atc Ile	act Thr	gaa Glu	atc Ile	agg Arg 110	aaa Lys	gaa Glu	336
gaa Glu	tta Leu	ggc Gly 115	ata	agc Ser	tct Ser	caa Gln	gat Asp 120	ccc Pro	aga Arg	atg Met	gtg Val	gtt Val 125	tca Ser	gcg Ala	ctc Leu	384
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Val	at a	aag Lys	att Ile	agc Ser	gac Asp 150	аσσ	ttg Leu	cac His	aac Asn	atg Met 155	ctc Leu	acc Thr	tta Leu	gac Asp	gcc Ala 160	480
145 ttg Leu	cct Pro	cat His	gac Asp	aag Lys 165	caa	gtg Val	cgt Arg	att Ile	tct Ser 170	aaa	gag Glu	act Thr	cta Leu	gcg Ala 175	gtg Val	528
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tta Leu	gaa Glu	gac Asp 195	aaσ	agc Ser	ttt Phe	tat Tyr	tat Tyr 200	att	tat Tyr	cca Pro	gaa Glu	gag Glu 205	tat Tyr	aaa Lys	aat Asn	624
atc Ile	Lys	gaa Glu	tat Tyr	ttg Leu	cac His	aaa Lys 215	aac	aag Lys	cag Gln	tct Ser	tta Leu 220	ctc Leu	tta Leu	aag Lys	ctc Leu	672
Asn	Ala	ttt	gcg Ala	agc Ser	aag Lys 230	tta	gaa Glu	aaa Lys	aaa Lys	ctt Leu 235	ttt	gat	agt Ser	ggg	ttt Phe 240	720
225 ago Ser	cat	tcg Ser	gat Asp	Phe	aaa	ctc Leu	gtt Val	aca Thr	agg Arg 250	gtg	aaa Lys	cgc Arg	cct Pro	tat Tyr 255	tct Ser	768
atc Ile	tat Tyr	ctt Leu	Lys	Met	caa Gln	cga Arg	aag Lys	Gly	qcq	gtt Val	aat Asn	att Ile	gat Asp 270	gaa Glu	att Ile	816
ttg Lev	gac Asp	Leu	Leu	σcc	att Ile	agg Arg	Ile	Leu	ttg Leu	aaa Lys	aac Asn	Pro	att Ile	gat	tgc Cys	864
tat Tyr	aaa Lys	275 gtt Val	tta	ggg Gly	att Ile	Ile	280 cat His	tta	aat Asn	ttc Phe	Lys	Pro	att	gtc Val	tct Ser	912
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Ile Val His Pro Ile Cys Val Ala Ser Leu Val Ala Phe Cys Gly Gly
                         55
Asp Glu Ala Met Val Cys Ala Ala Leu Leu His Asp Val Val Glu Asp
                     70
Thr Pro Cys Lys Ile Glu Thr Ile Glu Gln Glu Phe Gly Gln Asp Val
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Ala Asn Leu Val Asp Ala Leu Thr Lys Ile Thr Glu Ile Arg Lys Glu
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            100
Glu Leu Gly Val Ser Ser Gln Asp Pro Arg Met Val Val Ser Ala Leu
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                            120
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 Thr Phe Arg Lys Ile Leu Ile Ser Ala Ile Gln Asp Pro Arg Ala Leu
                                            140
                        135
Val Val Lys Ile Ser Asp Arg Leu His Asn Met Leu Thr Leu Asp Ala
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 Leu Pro His Asp Lys Gln Val Arg Ile Ser Lys Glu Thr Leu Ala Val
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 Tyr Ala Pro Ile Ala Ser Arg Leu Gly Met Ser Ser Ile Lys Asn Glu
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 Leu Glu Asp Lys Ser Phe Tyr Tyr Ile Tyr Pro Glu Glu Tyr Lys Asn
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 Ile Lys Glu Tyr Leu His Lys Asn Lys Gln Ser Leu Leu Leu Lys Leu
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 Asn Ala Phe Ala Ser Lys Leu Glu Lys Lys Leu Phe Asp Ser Gly Phe
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 Ser His Ser Asp Phe Lys Leu Val Thr Arg Val Lys Arg Pro Tyr Ser
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 Leu Asp Leu Leu Ala Ile Arg Ile Leu Leu Lys Asn Pro Ile Asp Cys
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  att aag gtc agt ctc cct aac gct aaa aat gcg gaa aaa tcc cag cca
   1
                                                                    96
  Ile Lys Val Ser Leu Pro Asn Ala Lys Asn Ala Glu Lys Ser Gln Pro
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ttc Phe	gta Val	35 gat Asp	gac Asp	aaa Lvs	ccg Pro	atg Met	40 aat Asn	tta Leu	gaa Glu	gct Ala	ttg Leu	45 agc Ser	gct Ala	gta Val	gtc Val	192
	50 caa	-				55	•				60					240
Lys 65	Gln	Thr	Asp	Pro	Lys 70	Thr	Leu	Ile	Asp	Leu 75	Lys	Ser	Asp	Lys	Ser 80	
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	Asp	35					40					45				
	Val 50 Gln	_				55					60					
65	Arg				70					75					80	
	His			85					90			200	_,_	95		
	nis )> 19		100	-,	-		-	105	<b>J</b>							
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	2> Di 3> He		bact	ter p	ylo	ri										
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ī	Ser	_		5					10					15		06
atg	aaa Lys	gcc	tat	acc	gca.	ttg	cta	aaa Lvs	aaa Lvs	Gln	gac	cga Ara	tac Tvr	gtc Val	tat Tvr	96
	ttg		20					25					30	•		144
Leu	Leu	Arg 35	Tyr	Leu	Pro	Ser	Arg 40	Tyr	Trp	Ala	Ser	Ile 45	Leu	Thr	Thr	
gcc	ctt	tat	gtc	aaa	tac	cct	gat	ttt	gac	gct	ttg	aaa	aag	ctt	ttg	192
	Leu 50	_				55					60					
gtg Val	tct Ser	tat Tyr	tat Tyr	tac Tyr	caa Gln	act Thr	tgg Trp	att Ile	gca Ala	gga Gly	ggc Gly	acg Thr	atc Ile	acg Thr	cgc Arg	240
65		_			70					75					80	000
atc Ile	aag Lys	caa Gln	acc Thr	agt Ser	atc Ile	aac Asn	att Ile	atc Ile	Lys	aac Asn	gtt Val	aaa Lys	agc Ser	Asn	aag Lys	288
agc	.gtt	gaa	acc	85 atc	aaa	gag	ctt	ata	.90 ttg	aat	agc	atc	gac	95 tct	tat	336

_		<b>01.</b>	Mh	T1.	Tue	Glu	T.e.n	Tle	Len	Asn	Ser	Ile	Asp	Ser	Tyr	
			100					105					110			
220	acc	ttt	ast	caa	tac	ctc	tat	aac	tta	tgg	gat	agc	tct	tct	gtt	384
Aen	Thr	Phe	Asp	Gln	Tyr	Leu	Tyr	Asn	Leu	Trp	Asp	26T	Ser	Ser	Val	
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tat	cat		aaa	taa	gtg	cgt	cct	gtc	tta	gcc	cta	gct	aat	tat	ttc	432
Tur	His	Ser	Lvs	Trp	Val	Arg	Pro	Val	Leu	Ala	Leu	Ala	Asn	Tyr	Phe	
	1 20					135					140					
ato		σat	gaa	σασ	aaa	CCC	cat	ttt	atc	gct	atg	gat	gcc	gaa	acc	480
Mot	Δla	Asp	Glu	Glu	Lvs	Pro	His	Phe	Ile	Ala	Met	Asp	Ala	Glu		
1 4 5					150					122					100	
	ata.	пап	cat	att	ttq	cca	caa	acg	CCC	aaa	aga	ggc	agt	Caa	tgg	528
Gla	Val	Glu	His	Ile	Leu	Pro	Gln	Thr	Pro	Lys	Arg	Gly	Ser	0.1.1.	Trp	
				165					170		•			113		
220	aca	σat	ttt	αac	aaa	gaa	aaa	aga	gaa	gaa	tgg	gta	aat	aat Aen	atc	576
Acn	Δla	Asp	Phe	Asp	Lys	Glu	Lys	Arg	Glu	Glu	Trp	Val	Asn	Asn	Ile	
			120					185					190			
aca	aat	tta		ctt	tta	aag	cgt	aaa	aag	aac	gcg	cat	gct	tta	aac	. 624
Ala	Asn	Leu	Thr	Leu	Leu	Lys	Arg	Lys	Lys	Asn	Ala	urs	Ala	Leu	Asn	
		105					200					200				650
aaa	gat	ttt	gat	gaa	aaa	aga	aaa	att	tat	gga	ggc	aaa	gac	acg	agc	672
61 v	Asp	Phe	Asp	Ğlu	Lys	Arg	Lys	Ile	Tyr	Gly	Gly	Lys	Asp	Thr	Ser	
	210					215					220					700
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Arg	Lvs	Trp	Asn	Glu	Lys	Ser	Leu	Gln	Glu	Arg	Tyr	Lys	Ser	Dea	Tyr	
				245					250					200		016
aac	act	atc	acg	cct	gtt	tta	cac	ata	gag	ggg	caa	gaa	gat	gat	דננ	816
Asn	Thr	Ile	Thr	Pro	Val	Leu	His	Ile	Glu	Gly	Gln	Glu	voh	Lap	Pne	
			260					265		•			270	,		027
gaa	gat	gat	ttt	gat	cta	gaa										837
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Asp	Ser	Lys	Lys	Asp	Ala	Cys	GIA	Pne	TTE	ıyı	GIU	110	. 501	15	Phe	
1				5		_		7	10		Der	) Arc	ጥህነ			
Met	: Lys	Ala	Tyr	Thr	Ala	Leu	Leu	груз	гÃ2	GIII	, vol	, mr	30	 )	Tyr	
			_20	) _		0	. 7	25	T~~	. Ala	Ser	· 11e			Thr	
Let	1 Lev			Leu	Pro	Ser	Arg	IÀT	ııp	, WTG	ber	45			Thr	
		35		_	-	D	40	Dha		. 11	T.o.			. Lev	Leu	
Ala	. Leu	Tyr	· Val	. Lys	ТУГ	PIC	Asp	rne	wah	ALG	60	 }			Leu	
	50			_	-1.	55	) 	Tla	71-	Glu			- T14	Thr	Ara	
Va]	Ser	Tyr	Tyr	Tyr			rirp	, IIe	Mia	75	( U.)				Arg 80	
65	<b>;</b>			_	70		<b>-1</b> -	. T1-	T 110			1.00	Sei	r Asr		
Ile	e Lys	Glr	Thr	: Ser	. 11e	ASI	, TT6	TIE	Э0 Эў	, Wei	. va.	Laye	,	95	Lys	
				. 85		<b>03.</b>	. 7					- T14	Ası			
Sea	c Val	Glu			: Lys	GIU	Lev	100	. Dec	L MOL	. 562		110	n n	Tyr	
			100	)		•	. m	105	) . Tas		. Acr	S 601			- Val	
Ası	n Thi	: Phe	a Asp	Glr	Tyr	Let	Tyr	ASI	Leu	ı ırt	, wai	125	. <i>De.</i>		. Val	
		115	:				120	)				12.	,			
Ty	r His	Sei	Lys	Trp	val	. Arc	Pro	val	. rer	I ATS	144	, v vrc	. ASI		Phe	
	120	١				13:	<b>.</b>				141	,				
Me	t Ala	a Asp	Glu	ı Glu	Lys	Pro	HIS	: Pne	: 116	155	1 1781 :	. nai	, MT	الدوال	Thr 160	
	_				150	1				135	,				00	
7.7	5					_		. m-	n		, n-	. 61.	, 50	r Gl.	1 Trp	

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170
Asn Ala Asp Phe Asp Lys Glu Lys Arg Glu Glu Trp Val Asn Asn Ile
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Ala Asn Leu Thr Leu Leu Lys Arg Lys Lys Asn Ala His Ala Leu Asn
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Gly Asp Phe Asp Glu Lys Arg Lys Ile Tyr Gly Gly Lys Asp Thr Ser
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Lys Val Ile Ser Cys Tyr Asp Ile Thr Lys Glu Leu Tyr Ser Asn Tyr
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Arg Lys Trp Asn Glu Lys Ser Leu Gln Glu Arg Tyr Lys Ser Leu Tyr
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Gly Ile Lys Leu Asn Tyr Val Glu Ala Val Ala Leu Ile Ser Ala His
                                 25
att atg gaa gaa gcg aga gct ggt aaa aag act gcg gct gaa ttg atg
                                                                   144
Ile Met Glu Glu Ala Arg Ala Gly Lys Lys Thr Ala Ala Glu Leu Met
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caa gaa ggg cgc act ctt tta aaa ccg gat gat gtg atg gat ggc gtg
                                                                   192
Gln Glu Gly Arg Thr Leu Leu Lys Pro Asp Asp Val Met Asp Gly Val
                         55
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                                                                   240
Ala Ser Met Ile His Glu Val Gly Ile Glu Ala Met Phe Pro Asp Gly
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aca aaa ctc gta acc gtg cat acc cct att gag gcc aat ggt aaa tta
                                                                   288
Thr Lys Leu Val Thr Val His Thr Pro Ile Glu Ala Asn Gly Lys Leu
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gtt cct ggt gag ttg ttc tta aaa aat gaa gac atc act atc aac gaa
Val Pro Gly Glu Leu Phe Leu Lys Asn Glu Asp Ile Thr Ile Asn Glu
                                105
ggc aaa aaa gcc gtt agc gtg aaa gtt aaa aat gtt ggc gac aga ccg
Gly Lys Lys Ala Val Ser Val Lys Val Lys Asn Val Gly Asp Arg Pro
                            120
gtt caa atc ggc tca cac ttc cat ttc ttt gaa gtg aat aga tgc tta
                                                                   432
Val Gln Ile Gly Ser His Phe His Phe Phe Glu Val Asn Arg Cys Leu
                                             140
                        135
    130
gac ttt gac aga gaa aaa act ttc ggt aaa cgc tta gac att gcg agc
                                                                   480
Asp Phe Asp Arg Glu Lys Thr Phe Gly Lys Arg Leu Asp Ile Ala Ser
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ggg aca gcg gta agg ttt gag cct ggc gaa gaa aaa tcc gta gaa ttg
                                                                   528
Gly Thr Ala Val Arg Phe Glu Pro Gly Glu Glu Lys Ser Val Glu Leu
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                                    170
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                                                                   576
Ile Asp Ile Gly Gly Asn Arg Arg Ile Phe Gly Phe Asn Ala Leu Val
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            180
gat agg caa gca gac aac gaa agc aaa aaa att gct tta cac aga gct
Asp Arg Gln Ala Asp Asn Glu Ser Lys Lys Ile Ala Leu His Arg Ala
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aaa gag cgt ggt ttt cat ggc gct aaa agc gat gac aac tat gta aaa
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Gln Glu Gly Arg Thr Leu Leu Lys Pro Asp Asp Val Met Asp Gly Val
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Ala Ser Met Ile His Glu Val Gly Ile Glu Ala Met Phe Pro Asp Gly
                                         75
                     70
 65
Thr Lys Leu Val Thr Val His Thr Pro Ile Glu Ala Asn Gly Lys Leu
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                 85
Val Pro Gly Glu Leu Phe Leu Lys Asn Glu Asp Ile Thr Ile Asn Glu
                                                     110
                                105
            100
Gly Lys Lys Ala Val Ser Val Lys Val Lys Asn Val Gly Asp Arg Pro
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                            120
        115
Val Gln Ile Gly Ser His Phe His Phe Phe Glu Val Asn Arg Cys Leu
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                       . 135.
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Asp Phe Asp Arg Glu Lys Thr Phe Gly Lys Arg Leu Asp Ile Ala Ser
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Gly Thr Ala Val Arg Phe Glu Pro Gly Glu Glu Lys Ser Val Glu Leu
                                     170
                165
Ile Asp Ile Gly Gly Asn Arg Arg Ile Phe Gly Phe Asn Ala Leu Val
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                                 185
            180
Asp Arg Gln Ala Asp Asn Glu Ser Lys Lys Ile Ala Leu His Arg Ala
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                            200
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Thr Ile Lys Glu
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                  5
 ago toa aga aco cao att ata gtg ogo gat ttg caa ggo aat gaa ogo
                                                                    96
 Ser Ser Arg Thr His Ile Ile Val Arg Asp Leu Gln Gly Asn Glu Arg
 gtg tta agc aat gaa gag att caa aag ctc atc aaa gaa gaa gaa gct
 Val Leu Ser Asn Glu Glu Ile Gln Lys Leu Ile Lys Glu Glu Glu Ala
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 Lys Ile Asp Asn Gly Thr Ser Lys Leu Val Gln Pro Asn Asn Gly Gly
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                     70
gcg gcg ggg gcg att tta ggg agt tat att ggt aat aag ctt ttc aat
                                                                   288
Ala Ala Gly Ala Ile Leu Gly Ser Tyr Ile Gly Asn Lys Leu Phe Asn
aac cet aat tac cag caa aac gee caa egg ace tac aaa tee eea caa
                                                                   336
Asn Pro Asn Tyr Gln Gln Asn Ala Gln Arg Thr Tyr Lys Ser Pro Gln
                                105
            100
get tac caa ege tet caa aat tee ttt tet aaa agt geg eee agt get
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Ala Tyr Gln Arg Ser Gln Asn Ser Phe Ser Lys Ser Ala Pro Ser Ala
                            120
        115
tca agc atg ggc gga gcg agt aag gga cag agc ggg ttt ttt ggc tct
                                                                   432
Ser Ser Met Gly Gly Ala Ser Lys Gly Gln Ser Gly Phe Phe Gly Ser
                                            140
                        135
agt agg cct act agt tca ccg gcg gta agc tct ggg aca agg ggc ttt
                                                                   480
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                    150
145
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Asn Ser
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                             40
Lys Ile Asp Asn Gly Thr Ser Lys Leu Val Gln Pro Asn Asn Gly Gly
                         55
Ser Asn Glu Gly Ser Gly Phe Gly Leu Gly Ser Ala Ile Leu Gly Ser
                                         75
                     70
Ala Ala Gly Ala Ile Leu Gly Ser Tyr Ile Gly Asn Lys Leu Phe Asn
                                     90
                 85
Asn Pro Asn Tyr Gln Gln Asn Ala Gln Arg Thr Tyr Lys Ser Pro Gln
                                105
           100
Ala Tyr Gln Arg Ser Gln Asn Ser Phe Ser Lys Ser Ala Pro Ser Ala
                            120
        115
Ser Ser Met Gly Gly Ala Ser Lys Gly Gln Ser Gly Phe Phe Gly Ser
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                        135
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Asn Ser
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cat aag gtg agc ggc cat gcg tat ttt tcg ctc aaa gac agc cag tcg
His Lys Val Ser Gly His Ala Tyr Phe Ser Leu Lys Asp Ser Gln Ser
             20
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	ġtt	att	aaa	tgc	gtg	ctg	ttt	aaa	ggg	aac	gct	aac	agg	ctc	aaa	ttc	144
	Val	Ile	Lys	Cys	Val	Leu	Phe		Gly	Asn	Ala	Asn	Arg 45	Leu	Lys	Phe	
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	Ala	Leu	Lys	Glu	Gly	Gln	Glu	Val	Val	Val	Phe	Gly	Gly	Ile	Ser	Val	
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y	12ء	101	, , , , , ,	, I.e.	ı Ála	TVI	: Sei	. Val	LTy	: Ile	e Arg	g Sei	. Ası	n Phe		
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aaa	gto	gc	cat	: כנו	. gc	ay	. 999	, m	e Tan	, 61.	 _ ጥኮ	r I.ve	, I,e	u Sei	r Thr	
Lys	Va]	Ala	a His	Phe	Ala	se:	: GT)	Ty	. net	ודמי	1 111	יצעי	اتادد		r Thr	

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Arg Glu Ile Gly Val Pro Ala Ile Val Gly Val Ser Gly Ala Thr Asp
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Ser Leu Tyr Thr Gly Met Glu Ile Thr Val Ser Cys Ala Glu Gly Glu
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	_	213	01	Ser	7.00	Non.	TOU	Thr	Gln	T.eu	Thr	Leu	Gly	Val	Asp	
Phe		lle	GIĀ	Ser	ASII	VOE	Dea	1111	U 1		300		•		<u>-</u> .	
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Phe Val Arg His Ala Lys Phe Arg Gln Asp Pro Ile Asn Asn Lys Leu
gat aca gag agt ggg aaa att caa att ttt tct caa aaa tgc gcg gat
Asp Thr Glu Ser Gly Lys Ile Gln Ile Phe Ser Gln Lys Cys Ala Asp
                     70
 65
ttt aaa ctg gcc gat ttt aaa ggg cat cct act tgg ttt gag cca gct
                                                                   288
Phe Lys Leu Ala Asp Phe Lys Gly His Pro Thr Trp Phe Glu Pro Ala
gag tgg cta ggc tct aaa atg gct gag att tat ccg ttc cat tta atc
Glu Trp Leu Gly Ser Lys Met Ala Glu Ile Tyr Pro Phe His Leu Ile
            100
                                105
tot cog cac cca aaa tac cgt gtc aat tca cag ctt gat aac act tgg
Ser Pro His Pro Lys Tyr Arg Val Asn Ser Gln Leu Asp Asn Thr Trp
                                                125
                            120
gtt agg aat gtg tat aaa att caa ggc aga gag cct gta atg atc aat
Val Arg Asn Val Tyr Lys Ile Gln Gly Arg Glu Pro Val Met Ile Asn
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Leu Tyr Glu Lys Ser Asp Gly Pro Thr Leu Lys Ser Phe Asp Gln Phe
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Trp Arg Asp Gly Phe Val Glu Phe Glu Ile Pro Glu Asn Ala Arg Lys
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Phe Val Arg His Ala Lys Phe Arg Gln Asp Pro Ile Asn Asn Lys Leu
Asp Thr Glu Ser Gly Lys Ile Gln Ile Phe Ser Gln Lys Cys Ala Asp
Phe Lys Leu Ala Asp Phe Lys Gly His Pro Thr Trp Phe Glu Pro Ala
Glu Trp Leu Gly Ser Lys Met Ala Glu Ile Tyr Pro Phe His Leu Ile
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            100
Ser Pro His Pro Lys Tyr Arg Val Asn Ser Gln Leu Asp Asn Thr Trp
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                            120
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aca gat att gac gat aag atc atc aac aaa gcc cta aaa gaa aac aaa
Thr Asp Ile Asp Asp Lys Ile Ile Asn Lys Ala Leu Lys Glu Asn Lys
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age att caa gaa tta age age att tat att gaa tet tae aeg agg gat
Ser Ile Glu Glu Leu Ser Ser Ile Tyr Ile Glu Ser Tyr Thr Arg Asp
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ttg aac gct ttg aac gtg aaa aaa ccc agc cta gag cct aaa gcg agc
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Leu Asn Ala Leu Asn Val Lys Lys Pro Ser Leu Glu Pro Lys Ala Ser
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 gag tat tta gac gct atg gtg ggc atg att gaa acg ctt tta gaa aaa
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 Glu Tyr Leu Asp Ala Met Val Gly Met Ile Glu Thr Leu Leu Glu Lys
                                          75
                      70
 aat atc gct tat cag gtc tct aat ggg gat att tat tta gac acg agc
                                                                    288
 Asn Ile Ala Tyr Gln Val Ser Asn Gly Asp Ile Tyr Leu Asp Thr Ser
                                      90
                  85
 aag gat aaa gat tac ggc tct ttg agc gtg cat aat agc agc att gaa
                                                                    336
 Lys Asp Lys Asp Tyr Gly Ser Leu Ser Val His Asn Ser Ser Ile Glu
                                 105
 ttt ggc cgt att ggt ttg gtg caa gaa aaa cgg ctt gag cag gat ttt
                                                                    384
 Phe Gly Arg Ile Gly Leu Val Gln Glu Lys Arg Leu Glu Gln Asp Phe
                                                 125
                             120
 gtg tta tgg aaa agc tat aag ggg gat aat gat gtg ggc ttt gat agc
                                                                    432
 Val Leu Trp Lys Ser Tyr Lys Gly Asp Asn Asp Val Gly Phe Asp Ser
                                             140
                         135
 cet tta ggc aaa ggg cgc cet ggc tgg cat ata gaa tgc tet agc atg
                                                                    480
 Pro Leu Gly Lys Gly Arg Pro Gly Trp His Ile Glu Cys Ser Ser Met
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145					150					155	•				160	
gtt	ttt	gaa	act	tta	gcg	ctc	act	aac	acc	ccc	tat	caa	att	gat	atc	528
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cat	gca	ggc	gga	gcg	gat	ttg	tta	ttc	ccc	cac	cat	gaa	aat	gaa	gcg	576
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tgc	caa	acc	cgt	tgc	gcc	ttt	ggc	gtg	gag	ctt	gcc	aaa	tat	tgg	atg	624
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								agt								816
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								ggg								864
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								agc								960
	Lys	Ala	Leu	Ser		ren	GIU	Ser	мет		Ser	Ser	Thr	ASN		
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aaa	ttg	gat	Caa	aac	CCL	aaa	aac	aag Lys	DI.	LLA	Tue	Glu	Glu	Tla	Lua	1008
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gcg	aat	ttg	aaa	Dha	ata	gaa	Clu	ctg Leu	Lou	gge	TIA	999	Pho	Two	yac Nen	1056
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CCT	agc	gcc	Tur	Pho	Caa	LLd	Glu	gtg Val	Sor	Glu	Sor	Glu	Lve	Gln	Glu	1104
		355	_		GIII	Deu	360	V	Jer	GIU	Ser	365		0111	010	1117
	Glu		aag	a												1111
	370		Lys													
)> 17															
	L> 37 2> PE															
			bact	.ar r	ים נעי	-i										
)> 17		Dace	.er j	, y I O I	•										•
Arg	Thr	Leu	Glu	Leu 5	Ser	Gly	Tyr	Glu	Val	Met	Leu	Val	Arg	Asn 15	Phe	
_	Asp	Ile	Asp 20	Asp	Lys	Ile	Ile	Asn 25		Ala	Leu	Lys	Glu 30	_	Lys	
Ser	Ile	Gln 35		Leu	Ser	Ser	Ile 40	Tyr	Ile	Glu	Ser	Tyr 45	Thr	Arg	Asp	
Leu	Asn 50		Leu	Asn	Val	Lys 55		Pro	Ser	Leu	Glu 60		Lys	Ala	Ser	
Glu		Leu	Aso	Ala	Met		Glv	Met	Ile	Glu		Leu	Leu	Glu	Lvs	
65	_				70			Gly		75					80	
ASN	TTE	VIQ	TAT	85	491	O-CI	noil	OT A	90	-1-	- y -	Jeu	٠.٠٠	95	J-12	
Lys	Asp	Lys	Asp		Gly	Ser	Leu	Ser		His	Asn	Ser	Ser		Glu	

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105
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Phe Gly Arg Ile Gly Leu Val Gln Glu Lys Arg Leu Glu Gln Asp Phe
                                                125
                            120
Val Leu Trp Lys Ser Tyr Lys Gly Asp Asn Asp Val Gly Phe Asp Ser
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                        135
Pro Leu Gly Lys Gly Arg Pro Gly Trp His Ile Glu Cys Ser Ser Met
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Val Phe Glu Thr Leu Ala Leu Thr Asn Thr Pro Tyr Gln Ile Asp Ile
                                    170
               165
His Ala Gly Gly Ala Asp Leu Leu Phe Pro His His Glu Asn Glu Ala
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           180
Cys Gln Thr Arg Cys Ala Phe Gly Val Glu Leu Ala Lys Tyr Trp Met
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His Asn Gly Phe Val Asn Ile Asn Asn Glu Lys Met Ser Lys Ser Leu
                                            220
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Gly Asn Ser Phe Phe Val Lys Asp Ala Leu Lys Asn Tyr Asp Gly Glu
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                    230
Ile Leu Arg Asn Tyr Leu Leu Gly Val His Tyr Arg Ser Val Leu Asn
                                    250
                245
Phe Asn Glu Glu Asp Leu Leu Val Ser Lys Lys Arg Leu Asp Lys Ile
                                                     270
                                265
Tyr Arg Leu Lys Gln Arg Val Leu Gly Thr Leu Gly Gly Ile Asn Pro
                                                 285
                            280
Asn Phe Lys Lys Glu Ile Leu Glu Cys Met Gln Asp Asp Leu Asn Val
                                            300
                        295
Ser Lys Ala Leu Ser Val Leu Glu Ser Met Leu Ser Ser Thr Asn Glu
                                         315
                    310
Lys Leu Asp Gln Asn Pro Lys Asn Lys Ala Leu Lys Gly Glu Ile Leu
                                     330
                325
Ala Asn Leu Lys Phe Ile Glu Glu Leu Leu Gly Ile Gly Phe Lys Asp
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Pro Ser Ala Tyr Phe Gln Leu Gly Val Ser Glu Ser Glu Lys Gln Glu
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Ile Glu Asn Lys
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.aac cat aaa aaa gaa aga gaa aaa aga gaa gtt aaa caa gaa gaa gaa
                                                                    96
 Asn His Lys Lys Glu Arg Glu Lys Arg Glu Val Lys Gln Glu Glu Glu
                                  25
             20
 att aaa gac atc aat ctg caa tta agc aaa atc aga gac agc ctg aaa
 Ile Lys Asp Ile Asn Leu Gln Leu Ser Lys Ile Arg Asp Ser Leu Lys
                              40
 ctc att caa aac atg ttt tgg gat gag aaa aac ccc aat tct att aat
 Leu Ile Gln Asn Met Phe Trp Asp Glu Lys Asn Pro Asn Ser Ile Asn
                          55
 atc cet caa gaa ttt gca gaa att tac aaa etg gee aaa caa agt ggg
 Ile Pro Gln Glu Phe Ala Glu Ile Tyr Lys Leu Ala Lys Gln Ser Gly
                                          75
                     70
 atg aaa ccc agc cat tta gat gaa atc atg caa ttg agc ctg gaa ttg
 Met Lys Pro Ser His Leu Asp Glu Ile Met Gln Leu Ser Leu Glu Leu
                  85
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atg cct tta cgc atg cgc gaa aat tcc gta acg att aag cgt tat ttt
Met Pro Leu Arg Met Arg Glu Asn Ser Val Thr Ile Lys Arg Tyr Phe
                                105
            100
aga gaa gtg ttg cgc aaa atg atc ttg tgt tgc cct gaa gat ttg aat
                                                                   384
Arg Glu Val Leu Arg Lys Met Ile Leu Cys Cys Pro Glu Asp Leu Asn
                            120
tta agg caa aaa cgc atc tta atg ctt gta ggg cca aca ggc gtg ggg
                                                                   432
Leu Arg Gln Lys Arg Ile Leu Met Leu Val Gly Pro Thr Gly Val Gly
    130
                        135
aaa acg acg act tta gct aaa tta gcc gcg cgc tat tct agg atg tta
                                                                   480
Lys Thr Thr Thr Leu Ala Lys Leu Ala Ala Arg Tyr Ser Arg Met Leu
                                        155
                    150
145
gct aaa aaa tac aag gtg ggc att atc act tta gac aat tat cgc att
Ala Lys Lys Tyr Lys Val Gly Ile Ile Thr Leu Asp Asn Tyr Arg Ile
                165
                                    170
ggg gct ttg gag caa tta agc tgg tat gct aat aaa atg aaa atg agt
Gly Ala Leu Glu Gln Leu Ser Trp Tyr Ala Asn Lys Met Lys Met Ser
                                185
            180
ata gaa gcg gtg att gac gct aag gat ttt gct aaa gaa att gaa gcg
Ile Glu Ala Val Ile Asp Ala Lys Asp Phe Ala Lys Glu Ile Glu Ala
                                                205
                            200
        195
ttg gaa tac tgc gat ttt att tta gtg gat acg aca ggg cat tcg caa t 673
Leu Glu Tyr Cys Asp Phe Ile Leu Val Asp Thr Thr Gly His Ser Gln
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Glu Ala Asn Lys Gln Asp Ala Leu Leu Gln Ala Leu Lys Asp Glu Ala
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Leu Ile Gln Asn Met Phe Trp Asp Glu Lys Asn Pro Asn Ser Ile Asn
                         55
Ile Pro Gln Glu Phe Ala Glu Ile Tyr Lys Leu Ala Lys Gln Ser Gly
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                                         75
Met Lys Pro Ser His Leu Asp Glu Ile Met Gln Leu Ser Leu Glu Leu
                                     90
                 85
Met Pro Leu Arg Met Arg Glu Asn Ser Val Thr Ile Lys Arg Tyr Phe
                                105
                                                    110
Arg Glu Val Leu Arg Lys Met Ile Leu Cys Cys Pro Glu Asp Leu Asn
                            120
                                                125
Leu Arg Gln Lys Arg Ile Leu Met Leu Val Gly Pro Thr Gly Val Gly
                                            140
                        135
Lys Thr Thr Thr Leu Ala Lys Leu Ala Ala Arg Tyr Ser Arg Met Leu
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Ala Lys Lys Tyr Lys Val Gly Ile Ile Thr Leu Asp Asn Tyr Arg Ile
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                                                         175
                165
Gly Ala Leu Glu Gln Leu Ser Trp Tyr Ala Asn Lys Met Lys Met Ser
                                185
                                                    190
            180
Ile Glu Ala Val Ile Asp Ala Lys Asp Phe Ala Lys Glu Ile Glu Ala
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Leu Glu Tyr Cys Asp Phe Ile Leu Val Asp Thr Thr Gly His Ser Gln
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    210
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 Asp Tyr Lys Asp Leu Asp Met Leu Lys His Thr Leu Ser Glu
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 Asp Tyr Lys Asp Leu Asp Met Leu Lys His Thr Leu Ser Glu
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 Glu Arg Leu Glu Lys Glu Ile Glu Val Ile Thr Asn Met Lys Phe Pro
                                       10
 ggg tat atg ctg att gtg tgg gat ttt atc cgt tat gct aag gaa atg
                                                                     96
 Gly Tyr Met Leu Ile Val Trp Asp Phe Ile Arg Tyr Ala Lys Glu Met
                                  25
 ggc att cct gta ggg cct ggt agg ggg agt gcg gcc ggg agc ttg gtg
                                                                     144
 Gly Ile Pro Val Gly Pro Gly Arg Gly Ser Ala Ala Gly Ser Leu Val
                              40
          35
 get ttt get tta aaa ate acg gat att gae eet ttg aaa tae gat ttg
                                                                     192
 Ala Phe Ala Leu Lys Ile Thr Asp Ile Asp Pro Leu Lys Tyr Asp Leu
                          · 55
                                               60
 ctc ttt gaa agg ttt tta aac ccc gaa aga atc agc atg cct gat a
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 Leu Phe Glu Arg Phe Leu Asn Pro Glu Arg Ile Ser Met Pro Asp
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 Gly Tyr Met Leu Ile Val Trp Asp Phe Ile Arg Tyr Ala Lys Glu Met
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                                  . 25
 Gly Ile Pro Val Gly Pro Gly Arg Gly Ser Ala Ala Gly Ser Leu Val
                               40
 Ala Phe Ala Leu Lys Ile Thr Asp Ile Asp Pro Leu Lys Tyr Asp Leu
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 Leu Phe Glu Arg Phe Leu Asn Pro Glu Arg Ile Ser Met Pro Asp
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ç	jat	200	m	31.	805	222	Luc	Thr	T.eu	Phe	Thr	Lvs	Ala	Glu	Phe	Ser	
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C	caa	aca	ttc	acc	ggg	caa	aac	agc	gcg	atc	gtt	דננ	999	31-	aaa	ayc Sor	777
(Sln	Thr	Phe 35	Thr	Gly	Gln	Asn	Ser 40	Ala	ше	Val	rne	45	WTG	пур		
:	ata	taa	acq	aqc	tta	agc	gat	gca	ccg	cag	tct	aac	acc	atc	att	cgc	192
1	lle	Trp	Thr	Ser	Leu	Ser	Asp 55	Ala	Pro	GIN	Ser	Asn 60	Ini	TTG	116	ALY	
4	-++	~~~	σac	aat	ааσ	gga	σca	aaa	agt	aat	gat	gcg	agc	ggg	cat	tgc	240
1	Phe	Gly	Asp	Asn	Lys	Gĺy 70	Åla	Gly	Ser	Asn	Asp 75	Ala	Ser	Gly	His	Cys 80	
	65				+ ~ ~		aac	+++	att	aca	aaa	cat	tat	qaa	gcg	caa	288
1	tgg	aat	ttg	Caa	Cur	Tla	Glu	Dha	Tle	Thr	Glv	His	Tvr	Ğlu	Ala	Gln	
	_				85					90					23		336
ŧ	aag	att	tac	atc	acc	ggt	agc	att	gaa	con	C1.	Den	Δra	Tle	tct	Ser	
	-			100					105					110	Ser		384
•	ggt	ggg	ggc	gcg	agc	ctt	aat	ttt	aac	ggg	CLL	caa	ggc	TIA	ctt	Lua	304
(Gly	Gly	Gly	Ala	Ser	Leu	Asn	Phe 120	Asn	GIY	Гéп	GIN	125	116	neu	Deu	430
	acq	aac	gcg	act	ttg	tat	aac	cgc	gcc	gct	ggc	acg	caa	agc	tcg	tct	432
١	Thr	Asn 130	Ala	Thr	Leu	Tyr	Asn 135	Arg	Ala	Ala	GTÀ	140	GIN	261	Ser	Ser	
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		ata	σас	gat	acc	qca	caa	aat	ggc	ggt	aac	cct	aat	ttc	agt Sar	ttc	528
	Phe	Ile	Asp	Asp	Thr 165	Ala	Gln	Asn	Gly	170	ASN	Pro	ASI	FIIE	175	riie	
		ant	++a	aat	cta	gat	ttt	tct	aac	agc	tct	ttt	aga	ggc	tat	gtg	576
	Asn	Ala	Leu	Asn 180	Leu	Asp	Phe	Ser	Asn 185	Ser	Ser	Phe	Arg	Gly 190	Tyr	Val	•
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	999 61 v	I.vs	Thr	Gln	Ser	Val	Phe	Lys	Phe	Asn	Ala	Lys	Asn	Ala	Ile	Ser	
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	ttc	acc	200	cor	Thr	Acn	Len	Ser	Ser	Glv	Leu	Tvr	Gln	Met	Gln	Ala	
		210					215		•			220					720
	aaa	agc	gtg	ttg	דננ	gac	aat	Con	aat Non	Lua	Sor	Val	Ser	Val	ggg Glv	Thr	
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	agc	agt	att	aaa	gcc	aat	gcg	atc	aat	CLL	605	Cla	Aen	Ala	tct	Tle	
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	Asn	Asp	Thr 275	Ser	Ser	Leu	Asn	Leu 280	Asn	Gln	Ser	Thr	11e 285	ASII	Val	Ser	
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	Asn	Asn	Ala	Thr	Ile	Asn	Asp 295	Tyr	Ala	Ser	Leu	11e 300	ATa	Ser	Asn	Gly	
		290	فنفير				- 2J	ac-	att	22+	ttc			aca	aat	att	960
	tct	cac	CLL	aat	DF-	7-	999	yey ala	yet Val	Δen	Phe	Asn	Ser	Ala	Asn	Ile	
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	Thr	Thr	Ser	Leu	Asn	Asn	Ser	Ser	Ile	Val	Phe	Lys	Gly	Ala	val	Ser	

				225					330					335		
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Lęu	Gly	Gly	Gln 340	Phe	Asn	Leu	Ser	Asn 345	Asn	Ser	Ser	Leu	Asp 350	Phe	Gln	
aac	tct	agc	act	atc	acc	tct	aac	acg	gcg	ttt	aat	ttc	tat	gat	aac	1104
Gly	Ser	Ser 355	Ala	Ile	Thr	Ser	Asn 360	Thr	Ala	Phe	Asn	Phe 365	Tyr	Asp	Asn	•
gct	ttt	tct	caa	agc	ccc	atc	act	ttc	cat	caa	gcc	ctt	gac	att	aaa	1152
Ala	Phe 370	Ser	Gln	Ser	Pro	Ile 375	Thr	Phe	His	Gln	Ala 380	Leu	Asp	Ile	Lys	
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385	Pro				390					395					400	1248
gtg	ctg Leu	gat	tta	aaa	aac	agc	cag	CEE	gtt V-1	Dhe	ggc	Den	Cln	6) 4	Ser	1240
Val	Leu	Asp	Leu	405	ASII	Ser	GIII	nea	410	rne	GIJ	r.op		415	001	
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Len	Asn	Ile	Ala	Asn	Ile	Asp	Leu	Leu	Ser	Asp	Leu	Asn	Āsp	Asn	Lys	
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gag	cgt	atc	agc	ttc	ttt	ggc	atg	cac	atc	aat	gac	ggg	att	tat T	gat	1392
	Arg 450					455					460					1440
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465	гÀг	ASI	GIII	IIII	470	Ser	FIIE	1111	non	475	Dou				480	
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Lvs	Ile	Thr	Glu	Ser	Phe	Lys	Asp	Asn	Gln	Leu	Ser	Val	Thr	Leu	Ser	•
-				485					490					495		
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Phe	Asn		GIn	Lys	vai	Tyr	520	Asn	Ala	Asn	GTÅ	525	IAT	DEI	ıyı	
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	Trp 50					55					60					•
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Phe Ile Asp Asp Thr Ala Gln Asn Gly Gly Asn Pro Asn Phe Ser Phe
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Asn Ala Leu Asn Leu Asp Phe Ser Asn Ser Ser Phe Arg Gly Tyr Val
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Gly Lys Thr Gln Ser Val Phe Lys Phe Asn Ala Lys Asn Ala Ile Ser
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Lys Ser Val Leu Phe Asp Asn Ser Asn Leu Ser Val Ser Val Gly Thr
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Ser Ser Ile Lys Ala Asn Ala Ile Asn Leu Ser Gln Asn Ala Ser Ile
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Ser His Leu Asn Phe Asn Gly Ala Val Asn Phe Asn Ser Ala Asn Ile
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Gly Ser Ser Ala Ile Thr Ser Asn Thr Ala Phe Asn Phe Tyr Asp Asn
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Ala Phe Ser Gln Ser Pro Ile Thr Phe His Gln Ala Leu Asp Ile Lys
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Ala Pro Leu Ser Leu Gly Gly Asn Leu Leu Asn Pro Asn Asn Ser Ser
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Val Leu Asp Leu Lys Asn Ser Gln Leu Val Phe Gly Asp Gln Gly Ser
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 Glu Arg Ile Ser Phe Phe Gly Met His Ile Asn Asp Gly Ile Tyr Asp
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 Ala Lys Asn Gln Thr Tyr Ser Phe Thr Asn Pro Leu Asn Asn Ala Leu
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cgc	acc	ctt	tta	Val	Glu	Aen	T.en	Thr	Glv	Asn	Ile	Thr	Val	Asp	Gly	
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		275		Asn			280					285				010
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Ile	Asn .370	Glu	Leu	Val	Val	Lys 375	Thr	Asn	Gly	Val	Ser 380	Vaĺ	ĞÎÿ	Ğlu	Tyr	
act	cat	ttt	age	даа	gat	ata	aac	agt	caa	tcq	CQC	atc	aat	acc	qtq	1200
Thr	His	Phe	Ser	Glu	Asp	Ile	Ğĺv	Ser	Gln	Ser	Arg	Ile	Asn	Thr	Val	
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Arg	Leu	Ğlu	Thr	Gly 405	Thr	Arg	Ser	Ile	Phe 410	Ser	Gly	Gly	Val	Lys 415	Phe	
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Asn	Ālā	Ála	Ăla	Met	Phe	Phe	Ser	Asn	Asn	Val	Asp	Ser	Ala	Thr	Gly	
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	530	Gln				535					540					
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		Thr				135					740		Ile		
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Thr				165					1/0				Ala	113	
			100					185					Gln 190		
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					200					393					Val 400 Phe
				A 10 5					410					710	
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		435					441	)				773			Lys Met
	AEC	١				455	j .				400	,			Gln
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			500	1				505	)				210		. Gly
		519	;				520	)				323	,		Gly Lvs
	626	`				535					340	,			Lys Asn
Asr 545	_	3 Glu	ı His	va.	550	) r re/	n nA;	, WTG	. wys	555	,		-,-		7 Asn 560

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Glu Ile Lys Ala Lys Val Ala Tyr Val Lys Ile Pro Gln Leu Glu Asp
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Leu Glu Asn Asn Pro Val Tyr Ile Gly Gln Ile Ile Gly Val Thr Tyr
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gat tta ttg ctg ttt gac gct gag ttt ttg gaa gcc aaa atc aaa gac
                                                                   192
Asp Leu Leu Phe Asp Ala Glu Phe Leu Glu Ala Lys Ile Lys Asp
                         55
ggg ttg gat aaa acc caa att gag ctt tta aac aag atg cct aaa tgg
                                                                   240
Gly Leu Asp Lys Thr Gln Ile Glu Leu Leu Asn Lys Met Pro Lys Trp
                                         75
aaa aag gtg gaa aaa gag ett tte aga geg act tat tat tae aag att
                                                                   288
Lys Lys Val Glu Lys Glu Leu Phe Arg Ala Thr Tyr Tyr Lys Ile
                                     90
                 85
aag ggc ata aaa gcg att att ccg tcc tta gaa gtg agc gcg ttt tcc
                                                                   336
Lys Gly Ile Lys Ala Ile Ile Pro Ser Leu Glu Val Ser Ala Phe Ser
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            100
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Asn Lys Asp Lys Tyr Ile Asp His Ser Ile Ala Pro Lys Val Thr Leu
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                            120
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cag gta acg gat ttg tcc aaa aac cct cgt tat gcg aat gtc atg gct
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Gln Val Thr Asp Leu Ser Lys Asn Pro Arg Tyr Ala Asn Val Met Ala
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aaa gat tta caa gtc ttg caa tac aaa acc aaa gat tat gac gat aaa
                                                                   480
Lys Asp Leu Gln Val Leu Gln Tyr Lys Thr Lys Asp Tyr Asp Asp Lys
                                         155
                    150
145
aac aat att ttg gtg atg gaa ata gcg ttc aaa gaa gcc act tgg gaa
                                                                   528
Asn Asn Ile Leu Val Met Glu Ile Ala Phe Lys Glu Ala Thr Trp Glu
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                165
gat ttt cac atc aaa gaa gcg atc aag caa ggg ttt gat aac gcc tct
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Asp Phe His Ile Lys Glu Ala Ile Lys Gln Gly Phe Asp Asn Ala Ser
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            180
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Leu Asn Gln Ile Lys Ala Lys Glu Gly Ser Val Phe Tyr Tyr Cys Val
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Lys Gly Ile Lys Ala Ile Ile Pro Ser Leu Glu Val Ser Ala Phe Ser
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Gln Val Thr Asp Leu Ser Lys Asn Pro Arg Tyr Ala Asn Val Met Ala
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Lys Asp Leu Gln Val Leu Gln Tyr Lys Thr Lys Asp Tyr Asp Asp Lys
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                    150
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Asp Phe His Ile Lys Glu Ala Ile Lys Gln Gly Phe Asp Asn Ala Ser
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                                185
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                                                                   96
Ile Glu Leu Ser Thr Val Asn Tyr Leu Ala Pro Leu Ile Phe Asn Leu
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gac aag cag ctc atg ggg caa gtg gtt ttg gat tct aac aaa tac cca
Asp Lys Gln Leu Met Gly Gln Val Val Leu Asp Ser Asn Lys Tyr Pro
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cac tac cat tta aga gag aat att cta agc cac acg cat gaa
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His Tyr His Leu Arg Glu Asn Ile Leu Ser His Thr His Glu
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Gly	Phe	Ile	Tyr 20	Glu	Ile	Ser	Glu	Phe 25	Met	Lys	Ala	Tyr	30	ATG	ren	
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	Lys	35					40					45				192
agg	tat	tgg	gcc	agc	att	tta	acg	act	gcc	Ctt	Tur	gtc Val	aaa T.ve	Tur	Pro	192
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-	Ile			85					90					90		
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Ile	Ile	Lys	Asn 100	Val	Lys	Ser	Asn	Lys 105	Ser	vaı	GIU	Thr	11e	гйа	GIU	
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cat	ttt	atc	gct	atg	gat	gcc	gaa	acc	caa	gtg	gag	cat	att	teg	CCa Pro	528
				165					170					1/2	Pro	E76
caa	acg	CCC	aaa	aga	ggc	agt	caa	tgg	aac	gcg	gat	Dhe	gac	aaa T.vs	gaa Glu	576
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ato	act Thr	aaa T.ve	Glu	T.e.ii	Tur	Ser	Asn	Tvr	Arq	Lys	Trp	Asn	Glu	Lys	Ser	
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ctc	caa	gag	cga	tac	aaa	tct	ttg	tat	aac	act	atc	acg	CCT	gtt	tta	816
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cac	ata	gag	ggg	caa	gaa	gat	gat	ttt	gaa	gat	gat	ttt	gat	cta	gaa	864
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Arg Tyr Trp Ala Ser Ile Leu Thr Thr Ala Leu Tyr Val Lys Tyr Pro
Asp Phe Asp Ala Leu Lys Lys Leu Leu Val Ser Tyr Tyr Tyr Gln .Thr
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Trp Ile Ala Gly Gly Thr Ile Thr Arg Ile Lys Gln Thr Ser Ile Asn
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Ile Ile Lys Asn Val Lys Ser Asn Lys Ser Val Glu Thr Ile Lys Glu
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Tyr Asn Leu Trp Asp Ser Ser Ser Val Tyr His Ser Lys Trp Val Arg
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Pro Val Leu Ala Leu Ala Asn Tyr Phe Met Ala Asp Glu Glu Lys Pro
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Gln Thr Pro Lys Arg Gly Ser Gln Trp Asn Ala Asp Phe Asp Lys Glu
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                                 185
Lys Arg Glu Glu Trp Val Asn Asn Ile Ala Asn Leu Thr Leu Leu Lys
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                            200
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Arg Lys Lys Asn Ala His Ala Leu Asn Gly Asp Phe Asp Glu Lys Arg
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Lys Ile Tyr Gly Gly Lys Asp Thr Ser Lys Val Ile Ser Cys Tyr Asp
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Ile Thr Lys Glu Leu Tyr Ser Asn Tyr Arg Lys Trp Asn Glu Lys Ser
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Leu Gln Glu Arg Tyr Lys Ser Leu Tyr Asn Thr Ile Thr Pro Val Leu
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tca cgc aaa aat agg gcg cga aat ttt atg cca aga atg cca aaa gat
                                                                   96
Ser Arg Lys Asn Arg Ala Arg Asn Phe Met Pro Arg Met Pro Lys Asp
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tcg cac tcg caa ggc ttt gag act tta agc att aat ttt gaa ggc acg
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Ser His Ser Gln Gly Phe Glu Thr Leu Ser Ile Asn Phe Glu Gly Thr
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                                                  45
         35
atg gag tgg agc gcg ttt ggg att tgg ctg agt ttg tta ttg cat caa
                                                                   192
Met Glu Trp Ser Ala Phe Gly Ile Trp Leu Ser Leu Leu Leu His Gln
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tac ggc aca cag att tta cgc atc aag ggg att att gac att gga agc
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Tyr Gly Thr Gln Ile Leu Arg Ile Lys Gly Ile Ile Asp Ile Gly Ser
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ggc ttt ttg gtg agt att aac ggc gtg atg cat gtc att tac ccg cct
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Gly Phe Leu Val Ser Ile Asn Gly Val Met His Val Ile Tyr Pro Pro
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aag cat att tta aag gat caa aac ggc tct aac ctc gtt ttt atc atg
                                                                   336
Lys His Ile Leu Lys Asp Gln Asn Gly Ser Asn Leu Val Phe Ile Met
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            100
cgc cat tta gag cgt gaa aaa atc tta aat tcc tta aag ggt ttt aag
                                                                   384
Arg His Leu Glu Arg Glu Lys Ile Leu Asn Ser Leu Lys Gly Phe Lys
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                                                                   417
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Tyr Gly Thr Gln Ile Leu Arg Ile Lys Gly Ile Ile Asp Ile Gly Ser
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                      70
65
Gly Phe Leu Val Ser Ile Asn Gly Val Met His Val Ile Tyr Pro Pro
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Lys His Ile Leu Lys Asp Gln Asn Gly Ser Asn Leu Val Phe Ile Met
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                                 105
             100
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 Gin Gin Asp Leu Lys Lys Ile Leu Gly Val Glu Glu Val Ile Met Leu
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 tcc aca agc ccc atg gaa tta cga tta gcc aat caa aag ctg ggc aat
 Ser Thr Ser Pro Met Glu Leu Arg Leu Ala Asn Gln Lys Leu Gly Asn
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 cgt ttc att aaa acc tta caa gcc atg aac gaa tta gac atg ggc gaa
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                 85
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Phe Phe Asn Ala Tyr Ala Gln Lys Thr Lys Asp Pro Thr His Ala Thr
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            100
age tat ggc gtt ttt gcg gca agt ttg ggg att gaa ttg aaa aag gct
                                                                   384
Ser Tyr Gly Val Phe Ala Ala Ser Leu Gly Ile Glu Leu Lys Lys Ala
                            120
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tta agg cat tat ctt tat gcg caa act tct aac atg gtg atc aac tgc
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145
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Ser Leu Gln Ser Pro Phe Asn Gln Leu Ile Glu Lys Thr Leu Glu Leu
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gac gaa agc cac ctg tgc acg gca agc gtt caa aac gac att aag gcg
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Asp Glu Ser His Leu Cys Thr Ala Ser Val Gln Asn Asp Ile Lys Ala
                                185
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                                          75
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                             120
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 Val Lys Ser Val Pro Leu Ser Gln Asn Asp Gly Gln Lys Ile Leu Leu
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act	ttc	aca	000	gat	agg	qtt	tat	atc	acc	ggt	aac	atg	atg	act	ggt	144
Thr	Phe	Thr 35	Ala	Asp	Arg	Val	Tyr 40	Ile	Thr	Gly	Asn	Met 45	Met	Thr	Gly	
		~~t	<b>C22</b>	acc	aat	aaa	aaa	aca	act	ttg	aat	ttt	gtg	ggc	gcg	192
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agc	gct	Lys	TIO	Aer.	Val	Ser	Gln	Ser	Asp	Phe	Tvr	Āsp	Trp	Thr	Gly	
Ser	Ala	Lys		MOII	101	001	· · · · ·	105				•	110		_	
		tat	100	+++	200	aat	aat	aac	att	ttt	σat	agc	ata	aat	ttc	384
ggg	ggg	Tyr	gat	Dho	The	Glv	Agn	Glv	Val	Phe	Asp	Ser	Val	Asn	Phe	
Gly	Gly		Asp	Pne	TIII	GIY	120	O.J	142			125				
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aac	aag	gct Ala	tat	man	Tue	Dho	Gln	Glv	Thr	Glu	Asn	Ser	Tvr	Asn	Phe	
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aaa	aac	acg Thr	aac	Dha	Ton	Nla	614	Acn	Phe	Lvs	Phe	Gln	Ğĺv	Lys	Thr	
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acc	att	gaa Glu	aaa	Con	yet val	Tan	Ser	Aen	Ala	Ser	Tvr	Thr	Phe	Āsp	Gly	
Thr	Ile	GIU	гÀг	261	Vai	Tea	261	nsp	170		-1-			175	_	
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acg	aat	aac Asn	acc	חשי	mb-	Glu	Aen	Luc	Phe	Asn	Asn	Glv	Ser	Phe	Asn	
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ttt	agt	Cat His	gca	gag	Cay	Thr	) ac	Ala	Phe	Asn	Asn	Asn	Ser	Phe	Asn	
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cat		++	aqt	ggq	gaa	aac	cct	agc	ggo	acg	cta	gta	aat	aag	gat	960
Dro	יער. יער נ	, Ile	Ser	Gĺv	Ğlu	Asn	Pro	Ser	Gly	Thr	Leu	Val	. Ası	ı Lys	, mp	•
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PCT/IB00/00603

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Asn	Gly	Leu	Thr	Tyr	Tyr	11e	гÀг	345	ASII	Lite	no		350			1101
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							Tyr 40					40				
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Ser	Gln			0 5					70							
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	Asn	Thr													Thr 160	
Thr	Ile			166					1/4	,						
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	~ 4 /	Sei	. Phe			71.	`					•			Asn	
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				r Pho	e Th										t Gln	
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Val Asn Val Ser Leu Asp Ser Leu Lys Ser Asp Arg Val Leu Lys Ile
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Val Asn Asp Asp Glu Ile Leu Glu Leu Leu Glu Tyr Ala Lys Asn Arg
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cat ata caa atc cgc tac att gaa ttt atg gaa aac acg cat gct aaa
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His Ile Gln Ile Arg Tyr Ile Glu Phe Met Glu Asn Thr His Ala Lys
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                                 105
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cat age gat gat ttt tgc caa tet tgc aat egt ate egt ttg get tet
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Lys Ile Tyr Thr Leu Glu Asn Gly Tyr Gln Phe Gly Ile Ile Ala Pro
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His Ser Asp Asp Phe Cys Gln Ser Cys Asn Arg Ile Arg Leu Ala Ser
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Asp Gly Lys Ile Cys Pro Cys Leu Tyr Tyr Gln Asp Ala Ile Asp Ala
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            180
Lys Glu Ala Ile Ile Asn Lys Asp Thr Lys Asn Ile Lys Arg Leu Leu
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Asn Ser
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 acc aac tot tta aaa atg act aaa caa gaa gtt aag gac gaa tac aaa
 Thr Asn Ser Leu Lys Met Thr Lys Gln Glu Val Lys Asp Glu Tyr Lys
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 cag caa gaa ggg aac cca gaa atc aaa gcc aaa atc cgc caa atg atg
 Gln Gln Glu Gly Asn Pro Glu Ile Lys Ala Lys Ile Arg Gln Met Met
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 cta aaa aac gcc acg aat aaa atg atg caa gaa atc cct aaa gcc aat
 Leu Lys Asn Ala Thr Asn Lys Met Met Gln Glu Ile Pro Lys Ala Asn
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 gtc gtg gtt act aac ccc acc cat tac gcc gtc gct ctc aaa ttt gat
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 Val Val Val Thr Asn Pro Thr His Tyr Ala Val Ala Leu Lys Phe Asp
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 gaa gaa cac cet gtg cet gtg gta gtg get aaa gge acg gat tat tta
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 Glu Glu His Pro Val Pro Val Val Ala Lys Gly Thr Asp Tyr Leu
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                  85
 gcc att agg att aag ggc atc gct aga gag cat gac ata gaa att ata
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 Ala Ile Arg Ile Lys Gly Ile Ala Arg Glu His Asp Ile Glu Ile Ile
                                105
            100
 gaa aat aaa acg ctc gcc aga gag ctt tat aga gat gtg aaa tta aac
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Glu Asn Lys Thr Leu Ala Arg Glu Leu Tyr Arg Asp Val Lys Leu Asn
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gct gcc ata cca gaa gaa ttg ttt gaa gcc gtg gcg ata gtc ttc gct
                                                                   432
Ala Ala Ile Pro Glu Glu Leu Phe Glu Ala Val Ala Ile Val Phe Ala
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caa gtg gct aaa tta gag caa gaa cgc caa aaa caa aag atc att aaa
Gln Val Ala Lys Leu Glu Gln Glu Arg Gln Lys Gln Lys Ile Ile Lys
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cct ctt
Pro Leu
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Gln Gln Glu Gly Asn Pro Glu Ile Lys Ala Lys Ile Arg Gln Met Met
Leu Lys Asn Ala Thr Asn Lys Met Met Gln Glu Ile Pro Lys Ala Asn
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Val Val Val Thr Asn Pro Thr His Tyr Ala Val Ala Leu Lys Phe Asp
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Glu Glu His Pro Val Pro Val Val Val Ala Lys Gly Thr Asp Tyr Leu
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Ala Ile Arg Ile Lys Gly Ile Ala Arg Glu His Asp Ile Glu Ile Ile
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                                105
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Glu Asn Lys Thr Leu Ala Arg Glu Leu Tyr Arg Asp Val Lys Leu Asn
                            120
        115
Ala Ala Ile Pro Glu Glu Leu Phe Glu Ala Val Ala Ile Val Phe Ala
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Pro Leu
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Thr Gly Arg Thr His Gln Ile Arg Val His Leu Lys His Ile Asn His
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ccc att ata ggc gat acg ctt tat aat aac gag cca agt tta gcc aaa
                                                                   96
Pro Ile Ile Gly Asp Thr Leu Tyr Asn Asn Glu Pro Ser Leu Ala Lys
                                 25
             20
cgc ttg atg ctc cat gca cat aaa atc gcg cta cta ggg tat gaa ttt
Arg Leu Met Leu His Ala His Lys Ile Ala Leu Leu Gly Tyr Glu Phe
                                                  45
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gaa gcg atc gct cct aaa gaa ttt gaa att
Glu Ala Ile Ala Pro Lys Glu Phe Glu Ile
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Pro Ile Ile Gly Asp Thr Leu Tyr Asn Asn Glu Pro Ser Leu Ala Lys
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Arg Leu Met Leu His Ala His Lys Ile Ala Leu Leu Gly Tyr Glu Phe
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        35
Glu Ala Ile Ala Pro Lys Glu Phe Glu Ile
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   50
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Gln Glu Met His Ile Leu Met Ile His Ile Leu Cys Asp Cys Ile Glu
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agg cat ttc gct cat aaa aat
Arg His Phe Ala His Lys Asn
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Arg His Phe Ala His Lys Asn
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Arg His Tyr Glu Thr Met Phe Ile Leu Lys Pro Thr Leu Val Glu Glu
                                      10
 gag att aaa tcc aag att gag ttt tat aaa gaa gtg atc act aag cat
                                                                    96
 Glu Ile Lys Ser Lys Ile Glu Phe Tyr Lys Glu Val Ile Thr Lys His
                                  25
             20
 cac ggc gtg att gaa acg agc ctg gat atg ggc atg cgt aat tta gct
 His Gly Val Ile Glu Thr Ser Leu Asp Met Gly Met Arg Asn Leu Ala
                                                   45
                              40
 tat gaa atc aaa aag cac aaa aga ggc tat tat tat gtg gcg tat ttc
                                                                    192
 Tyr Glu Ile Lys Lys His Lys Arg Gly Tyr Tyr Tyr Val Ala Tyr Phe
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 aaa gcg gag ccg tca atg att gta gag ctt gaa cga ttg tat cgc atc
                                                                    240
 Lys Ala Glu Pro Ser Met Ile Val Glu Leu Glu Arg Leu Tyr Arg Ile
                                          75
                      70
  65
 aat gaa gac gtg ttg cgt ttc att gtg atc aaa tac gaa agc aag aaa
                                                                    288
 Asn Glu Asp Val Leu Arg Phe Ile Val Ile Lys Tyr Glu Ser Lys Lys
                  85
 gaa gtg gaa gcg tgg cat gcg ttg gtg gat agg gct aat aaa aag cca
                                                                    336
 Glu Val Glu Ala Trp His Ala Leu Val Asp Arg Ala Asn Lys Lys Pro
                                 105
             100
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tcg cac gcc aaa gaa aaa cac gaa aaa acc gaa cac acg cat tct cac
Ser His Ala Lys Glu Lys His Glu Lys Thr Glu His Thr His Ser His
                            120
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cac aca gag gaa gca gaa agc gta gga tct cat agc gaa
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         35
Tyr Glu Ile Lys Lys His Lys Arg Gly Tyr Tyr Tyr Val Ala Tyr Phe
                         55
Lys Ala Glu Pro Ser Met Ile Val Glu Leu Glu Arg Leu Tyr Arg Ile
                     70
 65
Asn Glu Asp Val Leu Arg Phe Ile Val Ile Lys Tyr Glu Ser Lys Lys
                 85
Glu Val Glu Ala Trp His Ala Leu Val Asp Arg Ala Asn Lys Lys Pro
                                                    110
                                105
            100
Ser His Ala Lys Glu Lys His Glu Lys Thr Glu His Thr His Ser His
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                            120
His Thr Glu Glu Ala Glu Ser Val Gly Ser His Ser Glu
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                  5
atg agc gct gaa gaa gtg gaa gca gag att gaa cgg ctg ctg aac aaa
                                                                    96
Met Ser Ala Glu Glu Val Glu Ala Glu Ile Glu Arg Leu Leu Asn Lys
             20
cgc caa gaa gcc gat aaa gaa cga aga gct caa aaa aaa caa gaa gcc
Arg Gln Glu Ala Asp Lys Glu Arg Arg Ala Gln Lys Lys Gln Glu Ala
                                                  45
                              40
         35
aaa ccc aaa caa gaa gtt acc cca aca aaa gaa acc ccc aaa gcc cct
                                                                    192
Lys Pro Lys Gln Glu Val Thr Pro Thr Lys Glu Thr Pro Lys Ala Pro
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 Lys Thr Glu Thr Lys Ala
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 <211> 70
 <212> PRT
 <213> Helicobacter pylori
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 Met Ser Ala Glu Glu Val Glu Ala Glu Ile Glu Arg Leu Leu Asn Lys
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              20
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		_			_	<b>01</b>			71.	C1-	Tue	T.ve	Gln	Glu	Ala	
		35		Asp			40					40				
Lys	Pro 50	Lys	Gln	Glu	Val	Thr 55	Pro	Thr	Lys	Glu	Thr 60	Pro	гуs	Ala	PIO	
Lys		Glu	Thr	Lys												
65	> 21	1	•		70											
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	> DN															
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		)(	(798)	)												
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Tyr	Ser	Ile	Asp	Phe	Asp	Ser	Ala	Glu	His	Thr	Ser	Leu	Phe 30	He	Pro	
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atg	ccg	agt	gtt	gta Val	gcg	Ser	Asn	Val	His	Leu	Gln	Gly	Asn	His	Ala	
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Ser	_	Lys	Ser	Met	Leu	Asn	Phe	Gly	Val	Pro	1yr 60	Leu	GIII	Vai	Asp	
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CE					70					15		•			80	288
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				85					90					33		
σca	ato	agg	cgt	tat	gaa	aga	gac	gat	gcg	agc	gtg	gct	aac	att	gcc	336
Ala	Met	Ğĺÿ	Arg	Tyr	Glu	Arg	Asp	Asp	Ala	Ser	Val	Ala	Asn 110	He	Ala	
			100	gga	202	200	cct	105	gaa	agc	att	·cac		ttt	tat	384
aac	Cag	Leu	Lvs	Glv	Thr	Thr	Pro	Lys	Glu	Ser	Val	Arg	Asn	Phe	Tyr	
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Ala		Ile	Lys	His	GIU	135	Pro	гÃ2	Arg	GXII	140	****			Gly	•
222	130 gaa	aat	tta	cct	aag	cat	gag	agt	ttg	ccc	tgg	ttt	gca	acc	att	480
Lys	Glu	Asn	Leu	Pro	Lys	Arg	Glu	Ser	Leu	Pro	Trp	Phe	Ala	Thr	Ile 160	
1 4 5					150					TOO					100	528
tca	aaa	gag	agc	atg	Phe	gtg Val	Ser	Leu	Cvs	His	Ala	Cys	Gly	Ile	aaa Lys	
	_			165					170					1/5		
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Ser	Ala	Glu	Val	Gln	Gly	Leu	Lys	Leu	GTĀ	Gln	Asn	Ser	190	val	Lys	
		·	180	at a	~	ata	tat	185		gat	tca	ttt			ttt	624
aac	gct Ala	Pro	Ara	. Val	Glu	Val	Tyr	Leu	Lys	Asp	Ser	Phe	Leu	Ala	Phe	
		105					200					200				670
gat	ttt	caa	aat	aat	cac	aag	gaa	gtt	ttt	atc	ccg	ttg	aat	CGT	cat	672
Asp			Asn	Asn	His	Lys 215	GIU	val	rne	TTE	220	Ten	. non	9	His	
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Lvs	Asp	Met	Gln	Leu	Asp	Ser	Ála	Leu	Leu	Ala	Thr	Phe	Gly	Asp	VIG	
225	_				230					235					240	768
ttt	gcc	ctt	gtg	gat	ggt	agg	gat	tta	ggc	aat	Tac	gag Gl::	Ser	Lvs	ctt Leu	700
Phe	Ala	Leu	Val	Asp	GTĀ	Arg	дем	Leu	оту	กฮม	TAT	310		-,-	Leu	

				245					250					255		
ttt	<b>~</b> >>		ana		tcc	tat	acq	att	_							798
Phe	yaa Glu	Lys	Arg	Val	Ser	Tyr	Thr	Ile	val							
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Ala	Glu	Glu	Ser		Gly	Ser	Val	Ala	Lys 10	Tyr	Lys	ITE	GIU	A1a 15	GIN	
1 Tvr	Ser	Ile	Asp	5 Phe	Asp	Ser	Ala	Glu		Thr	Ser	Leu	Phe	Ile	Pro	
		Ser	20					2,5					30			•
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	EΛ	Lys				55					บบ					
	Leu	Lys	Ser	Thr	Gln 70	Lys	Lys	Gln	Val	His 75	Leu	Ser	Tyr	Glu	80 116	
65 Ala	Ser	Tyr	Gln	Leu 85	Asn	Glu	Arg	Ļeu	Phe 90		Thr	Ser	Asp	Phe 95	Val	
Ala	Met	Gly	Arg	Tyr	Glu	Arg	Asp	Asp 105		Ser	Val	Ala	Asn 110	Ile	Ala	
Asn	Gln	Leu	Lys	Gly	Thr	Thr	Pro 120		Glu	Ser	Val	Arg 125	Asn	Phe	Tyr	
Ala		115 Ile	Lys	His	Glu	Met 135	Pro	Lys	Arg	Gln	Lys 140	Ala	Leu	Glu	Gly	
Lvs	130 Glu	Asn	Leu	Pro	Lys	Arg	Glu	Ser	Leu	Pro	Trp	Phe	Ala	Thr	Ile	
145					150					122					100	
		Glu		165					1/0					1/3		
		Glu	180	Gln	Gly			185					130			
		Pro 195	Arg	Val			200					200				
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	Asp	Met	Gln	Leu	Asp 230	Ser	Ala	Leu	Leu	Ala 235	Thr	Phe	Gly	Asp	Ala 240	
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tgo	ate	y CCC - Dha	, yat . Ner	. 99C	, cat	Thr	His	Tvr	Leu	Asr	Lev	Val	Leu	Val	Asn	
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		c ata	gad	cto	tct	ggt	gto	cga	gaa	tgo	att	gaa	gaa	agc	gaa	96
Cys	Pr	o Ile	Glu	ı Let	ı Ser	Gly	, Val	. Arg	i GTA	Cys	3 116	: GIU	30	Ser	GIU	944
ggo	gt	g gat	gg:	g gca	gto	g agt	gaa	acc	gct	agt	tct	cat	tta	tgo	gtg	144
Gly	y Va.	l Asg 35	o Gly 5	/ Ala	a Val	. Sei	4(	TNI	: Ala	Ser	s Ser	His 45	, Dec	Cys	Val	170
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ata gat att gga ggg ggt agc acc gag tgc gcg ttg att gaa aaa ggc
                                                                   96
Ile Asp Ile Gly Gly Gly Ser Thr Glu Cys Ala Leu Ile Glu Lys Gly
                                                      30
                                 25
             20
aag att aag gac tta atc tcg ctt gat gtt ggg acg att cgc att aaa
Lys Ile Lys Asp Leu Ile Ser Leu Asp Val Gly Thr Ile Arg Ile Lys
                             40
         35
gaa atg ttt tta gac aaa gac tta gag gtc aaa ttg gct aaa gcc ttt
                                                                   192
Glu Met Phe Leu Asp Lys Asp Leu Glu Val Lys Leu Ala Lys Ala Phe
                                              60
                         55
atc caa aaa gaa gtc tct aaa ctg ccc ttt aaa cac aaa aac gcc ttt
                                                                   240
Ile Gln Lys Glu Val Ser Lys Leu Pro Phe Lys His Lys Asn Ala Phe
                                          75
                     70
ggg gtg ggg ggg acg atc aga gcg ttg agt aag gta ttg atg aaa cgc
                                                                   288
Gly Val Gly Gly Thr Ile Arg Ala Leu Ser Lys Val Leu Met Lys Arg
                                      90
                 85
ttt tgt tac cct att gat tct ttg cat ggc tat gaa ata gat gca cat
                                                                   336
Phe Cys Tyr Pro Ile Asp Ser Leu His Gly Tyr Glu Ile Asp Ala His
                                105
aaa aat tta gcg ttc att gaa aaa atc gtc atg ctc aaa gaa gat caa
Lys Asn Leu Ala Phe Ile Glu Lys Ile Val Met Leu Lys Glu Asp Gln
                                                 125
                            120
tta cgg ctt tta ggg gtg aat gaa gag cgt ttg gat agc atc agg agc
Leu Arg Leu Leu Gly Val Asn Glu Glu Arg Leu Asp Ser Ile Arg Ser
                        135
ggg gcg ttg att tta tca gtc gtt ttg gag cat tta aaa act tct tta
Gly Ala Leu Ile Leu Ser Val Val Leu Glu His Leu Lys Thr Ser Leu
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                    150
atg atc act agt ggg gtg ggg gtg aga ggc gtg ttt ttg agc gat
                                                                   528
Met Ile Thr Ser Gly Val Gly Val Arg Glu Gly Val Phe Leu Ser Asp
                165
 tta ttg cgc cat cat tac cat aaa ttc ccc ccc aat atc aac ccc tct
Leu Leu Arg His His Tyr His Lys Phe Pro Pro Asn Ile Asn Pro Ser
                                 185
            180
 ctc atc tct tta aaa gat cgc ttt ttg ccc cat gaa aag cac agc caa
 Leu Ile Ser Leu Lys Asp Arg Phe Leu Pro His Glu Lys His Ser Gln
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aag gtc aaa aaa gaa tgc gtg aaa ttg ttt gaa gcc tta tcg cct ttg
Lys Val Lys Lys Glu Cys Val Lys Leu Phe Glu Ala Leu Ser Pro Leu
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cat aaa ata gat gaa aaa tac ctt ttc cat tta aag att gcg ggg
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His Lys Ile Asp Glu Lys Tyr Leu Phe His Leu Lys Ile Ala Gly
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Lys Ile Lys Asp Leu Ile Ser Leu Asp Val Gly Thr Ile Arg Ile Lys
                                                  45
                              40
Glu Met Phe Leu Asp Lys Asp Leu Glu Val Lys Leu Ala Lys Ala Phe
                         55
Ile Gln Lys Glu Val Ser Lys Leu Pro Phe Lys His Lys Asn Ala Phe
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Gly Val Gly Gly Thr Ile Arg Ala Leu Ser Lys Val Leu Met Lys Arg
                                     90
                 85
Phe Cys Tyr Pro Ile Asp Ser Leu His Gly Tyr Glu Ile Asp Ala His
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                                105
Lys Asn Leu Ala Phe Ile Glu Lys Ile Val Met Leu Lys Glu Asp Gln
                            120
        115
Leu Arg Leu Leu Gly Val Asn Glu Glu Arg Leu Asp Ser Ile Arg Ser
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Gly Ala Leu Ile Leu Ser Val Val Leu Glu His Leu Lys Thr Ser Leu
                                         155
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Met Ile Thr Ser Gly Val Gly Val Arg Glu Gly Val Phe Leu Ser Asp
                                     170
                165
Leu Leu Arg His His Tyr His Lys Phe Pro Pro Asn Ile Asn Pro Ser
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            180
Leu Ile Ser Leu Lys Asp Arg Phe Leu Pro His Glu Lys His Ser Gln
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                             200
        195
Lys Val Lys Lys Glu Cys Val Lys Leu Phe Glu Ala Leu Ser Pro Leu
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 Met Leu Ala Leu Gly Gln Ala His Met Lys Lys Glu Tyr Val Leu
                                  25
 gcg tot ttt tac ttt gat gaa tac atc aag cgc ttt ggg act aag gac
                                                                   144
 Ala Ser Phe Tyr Phe Asp Glu Tyr Ile Lys Arg Phe Gly Thr Lys Asp
                             40
 aat gtg gat tat ttg act ttt tta aaa ttg caa tcg cat tat tac gct
 Asn Val Asp Tyr Leu Thr Phe Leu Lys Leu Gln Ser His Tyr Tyr Ala
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60
                         55
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Asn Arg Ala Ile Ala Asn Val Tyr Lys Lys Arg His Lys Pro Glu Gly
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	2> P) 3> U		haci	ter :	pylo	ri										
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His His Ala His Phe Leu Ala Ser Val Leu Asp Ala Leu Gin Asp 20 25 30	
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ATS TAL OTA Wall mas the tal oth win our cas the ant orly was near	

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Lue	Asn	Glv	Glu	Ala	His	Ser	Thr	Ğlu	Ğĺy	Leu	Gly	Thr	Val	Asn	Lys	
145	ADI.	0-,			150				•	155	_				160	
aca	aaa	caa	gac	att	qaa	tcq	ctt	tat	gaa	aag	atg	caa	aac	gcc	act	528
Thr	Glv	Gln	Asp	Ile	Ğlu	Ser	Leu	Tyr	Ğlu	Lys	Met	Gln	Asn	Ala	Thr	
	_			165					170					175		
tca	cta	aca	gac	tct	ctc	aac	caa	cgg	agc	aat	gaa	atc	act	caa	gtc	576
Ser	Leu	Ala	Āsp	Ser	Leu	Asn	Gln	Arg	Ser	Asn	Glu	Ile	Thr	Gln	Val	
			180					185					190			
att	tct	ttg	att	gat	gat	att	gca	gaa	caa	acc	aat	cta	tta	gcc	cta	624
Ile	Ser	Leu	Ile	Asp	Asp	Ile	Ala	Glu	Gln	Thr	Asn	Leu	Leu	Ala	Leu	
		195					200					205				
aat	qcc	qct	att	gag	gcc	gcg	cga	gcg	ggc	gag	cat	ggg	aga	ggg	ttt	672
Asn	Ála	Āla	Ile	Glu	Ala	Ala	Arg	Ala	Gly	Glu	His	Gly	Arg	Gly	Phe	
	210					215					220			•		
qcq	gtg	gtg	gct	gat	gag	gtg	aga	aaa	ctc	gct	gaa	aaa	acc	caa	aaa	720
Ala	Val	Val	Ala	Asp	Glu	Val	Arg	Lys	Leu	Ala	Glu	Lys	Thr	Gln	гĀ2	
225					230					235					240	
acc	act	aaa	gaa	atc	gct	gtt	gtc	gtt	aaa	agc	atg	caa	caa	gaa	gcg	768
Ala	Thr	Lys	Glu	Ile	Ala	Val	Val	Val	Lys	Ser	Met	Gln	Gln	GIU	Ala	
				245					250					255		
aac	gat	att	caa	acc	aat	acc	cac	gat	att	aat	tct	att	gta	agc	tct	816
Asn	Asp	Ile	Gln	Thr	Asn	Thr	His	Asp	Ile	Asn	Ser	Ile	Val	Ser	Ser	
			260					265					270			
att	aag	aac	gat	gtg	gaa	gag	ctt	aaa	tcc	acc	gta	aaa	aat	aac	atg	864
Tle	Lvs	Glv	Asp	Val	Glu	Glu	Leu	Lys	Ser	Thr	Val	Lys	Asn	Asn	Met	
	_	275					280					285				
att	att	aca	caa	gcg	gca	aaa	tac	acc	atc	tac	aat	atc	aat	aac	cgg	912
Tle	Val	Ala	Gln	Ála	Āla	Lys	Tyr	Thr	Ile	Tyr	Asn	Ile	Asn	Asn	Arg	
	290					295					300					
ata	ttt	tac	gat	ttq	gcc	aaa	ctt	gat	cat	gtg	gtc	ttt	aaa	aac	aat	960
3-3		- 3-		_	-			-			-		•			

205					310					312				Asn	320	
_ 4. 4.	+-+	aac	ata	att	ttt	aat	ctc	aat	tcc	ttt	gat	att	acc	agc	cat	1008
Leu	Tyr	Gly	Met	Val	Phe	Gly	Leu	Asn	330	Pne	Asp	116	IIII	335	urs	
	22+	tac	cat	++=	aac	aaa	taa	tat	tat	gag	ggc	gcg	ggc	aaa	gag	1056
Lys	Asn	Cys	Arg	Leu	Gly	Lys	Trp	Tyr 345	туг	GIU	GTÅ	MIG	350	шys	GIU	
		+00		act	tca	aac	tat	aga	qct	tta	gaa	agc	cac	cat	gca	1104
aat	רננ	Con	Aac Aan	Thr	Ser	Glv	Tvr	Ara	Ãla	Leu	Glu	Ser	His	His	Ala	
		255					360					202				1152
agc	gtg	cat	gct	gaa	gct	aat	gat	Tou	Wal	Tue	Δla	Val	Gln	gaa Glu	Asp	
	270					375					200			Glu		1200
cac	att	acc	gat	tca	aaa	tac	cta	gag	cat	aaa	gra	uic	LLA	Mot	gaa	
His	Ile	Thr	Asp	Ser	Lys	Tyr	Leu	GIU	His	гуs	vaı	ura	Dea	Mec	Glu 400	
20E					390					333						1248
gat	agt	gct	aaa	cat	gtt	aga	gaa	aat	att	gat	aag	atg	רבר	m	gaa	1440
Asp	Ser	Ala	Lys	His	Val	Arg	Glu	Asn	TTE	Asp	гÀг	mec	FIIE	415	Glu	
				405					410					410		1293
aaa	caa	gat	gaa	ctc	aat	aaa	atc	att	gaa	aaa	att.	caa	aaa	ggc		123.
Lvs	Gln	Asp	Glu	Leu	Asn	Lys	Ile	Ile	Glu	Lys	IIe	GIN	гуэ	GIY		
-4		_	420					425					430			
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	2> P															
		elic	obac	ter	pylo	ri								:		
	^ ^	20										_	_		<b>G3</b>	
Phe	Gly	Asn		5					10							
Ile	Ala		າດ					2.5						,	Asn	
		25					40					33			Val	
		Ser	Gly			55					טס				Ser	
	His	Phe			70					12	,				Ser _ 80	
Ty	Ser			25					90	ļ.				,,,		
			100	Ser	Cys			בנוו					,	,	Phe	
Lys	Thr	Phe 115	Cys	Ala	Ser	Leu	Lys 120	Glu	Gly	Let	ı Glu	125	Ala S	a Glr	ı Glu	
Se		Gln	Туг	Phe	His	Gln 135	Glu	Thr	Gly	Ala	Lev 140	ı Lev	ı Ası	n Ala	Ala	
	130	, 63.			uia	501	· ጥኮ፣	· Glu	Glv	Lei	ı Glv	, Thi	· Val	l Asr	1 Lys	
	_	) GTA	GIU	HIC	150	Jer			,	155	5				160	
14: Th:	r Gly	/ Glr	Asp	Ile	Glu	Ser	Lev	Tyr	Glu 170	Lys	Met	Glr	ASI	n Ala 175	Thr	
Se	r Let	ı Ala	Asp	165 Ser	Leu	Asr	Glr	Arg	Ser	Asr	ı Glı	ı Ile	Th:	r Gli	n Val	٠.
Ile	e Se	r Leu	180 11e	) e Asp	Asp	ıle	Ala	185 Glu	Glr	Thi	r Ası	n Let 205	ı Le		a Leu	
		3 0 5					7118					20.	,			
	01/	^				215	•				221	3			y Phe	
	a Va	l Val			231	1				23.	,				n Lys 240	
22	ጋ ጥሎ	r Tur	, G1:	1 T14	Ale	Val	[ Va]	[ Val	Lys	Se	r Met	t Gli	n Gl	n Gl	u Ala 5	
				24	5				250	,					_	
As	n As	p 116	e Gli	ותור מ	C ASI	ı Tni	. urs	, ust	, 414	, ,,,,,,					r Ser	

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265
            260
Ile Lys Gly Asp Val Glu Glu Leu Lys Ser Thr Val Lys Asn Asn Met
                                                285
                            280
Ile Val Ala Gln Ala Ala Lys Tyr Thr Ile Tyr Asn Ile Asn Asn Arg
                                            300
                        295
    290
Val Phe Cys Gly Leu Ala Lys Leu Asp His Val Val Phe Lys Asn Asn
                                        315
                    310
Leu Tyr Gly Met Val Phe Gly Leu Asn Ser Phe Asp Ile Thr Ser His
                                    330
                325
Lys Asn Cys Arg Leu Gly Lys Trp Tyr Tyr Glu Gly Ala Gly Lys Glu
                                345
            340
Asn Phe Ser Asn Thr Ser Gly Tyr Arg Ala Leu Glu Ser His His Ala
                            360
        355
Ser Val His Ala Glu Ala Asn Asp Leu Val Lys Ala Val Gln Glu Asp
                                             380
                        .375
    370
His Ile Thr Asp Ser Lys Tyr Leu Glu His Lys Val His Leu Met Glu
                                         395
                    390
Asp Ser Ala Lys His Val Arg Glu Asn Ile Asp Lys Met Phe Tyr Glu
                                     410
                405
Lys Gln Asp Glu Leu Asn Lys Ile Ile Glu Lys Ile Gln Lys Gly
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                                                                   48
Asp Leu Asn Ala Ile Leu Glu Asp Leu Asn Ser Lys Gln Leu Leu Pro
  1
gaa tac gct tac aag gtt tat ggc gca gtg gtg agt caa aat aaa gac
Glu Tyr Ala Tyr Lys Val Tyr Gly Ala Val Val Ser Gln Asn Lys Asp
                                 25
             20
ggc gtg tgg gtc ggc gat gaa gcc aaa acg aaa gcc aga aga aaa gaa
Gly Val Trp Val Gly Asp Glu Ala Lys Thr Lys Ala Arg Arg Lys Glu
                              40
         35
att ctt gaa aac aga aag gct aga tcc ata ccg gta aaa caa tgg atg
                                                                   192
Ile Leu Glu Asn Arg Lys Ala Arg Ser Ile Pro Val Lys Gln Trp Met
                                              60
                         55
gag caa gaa aga aac gct atc ctt gaa aaa gag gct tcc aaa cag gtt
                                                                   240
Glu Gln Glu Arg Asn Ala Ile Leu Glu Lys Glu Ala Ser Lys Gln Val
                                          75
                  . 70
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 aag cac atg tat gcg act agc ttt gat ctc tcg cct aag ttt ttg a
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Lys His Met Tyr Ala Thr Ser Phe Asp Leu Ser Pro Lys Phe Leu
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 Asp Leu Asn Ala Ile Leu Glu Asp Leu Asn Ser Lys Gln Leu Leu Pro
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 Glu Tyr Ala Tyr Lys Val Tyr Gly Ala Val Val Ser Gln Asn Lys Asp
                                  25
 Gly Val Trp Val Gly Asp Glu Ala Lys Thr Lys Ala Arg Arg Lys Glu
                              40
          35
 Ile Leu Glu Asn Arg Lys Ala Arg Ser Ile Pro Val Lys Gln Trp Met
                                              60
                          55
 Glu Gln Glu Arg Asn Ala Ile Leu Glu Lys Glu Ala Ser Lys Gln Val
```

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80
                                         75
                     70
Lys His Met Tyr Ala Thr Ser Phe Asp Leu Ser Pro Lys Phe Leu
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aga cgc aat caa aaa agc gca tca aag ttt atc aac tat ccc tct aag
Arg Arg Asn Gln Lys Ser Ala Ser Lys Phe Ile Asn Tyr Pro Ser Lys
                                     10
tto tto act cta tgc tat aat ctc tgt ttt aaa aca tta tgg aat gtt
                                                                   96
Phe Phe Thr Leu Cys Tyr Asn Leu Cys Phe Lys Thr Leu Trp Asn Val
                                                      30
             20
aga aga tat toa goa aaa ooc tto caa acc aac caa tot aaa gaa aga
Arg Arg Tyr Ser Ala Lys Pro Phe Gln Thr Asn Gln Ser Lys Glu Arg
                                                 45
                              40
         35
                                                                   163
aac cat tca agg aac gca t
Asn His Ser Arg Asn Ala
    50
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Arg Arg Asn Gln Lys Ser Ala Ser Lys Phe Ile Asn Tyr Pro Ser Lys
                                     10
  1
Phe Phe Thr Leu Cys Tyr Asn Leu Cys Phe Lys Thr Leu Trp Asn Val
                                 25
             20
Arg Arg Tyr Ser Ala Lys Pro Phe Gln Thr Asn Gln Ser Lys Glu Arg
                              40
         35
Asn His Ser Arg Asn Ala
     50
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<213> Helicobacter pylori
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gac gat ege teg ttt ttt ate act gat tet ege tae act caa gaa get
Asp Asp Arg Ser Phe Phe Ile Thr Asp Ser Arg Tyr Thr Gln Glu Ala
                                     10
  1
aaa gaa agc gtt cag cct aaa aat ggc gtt tta gcg gaa gtg gta gaa
                                                                    96
Lys Glu Ser Val Gln Pro Lys Asn Gly Val Leu Ala Glu Val Val Glu
                                 25
             20
tct agc gat tta gtg caa agc gcg att gat ttg att gtt aaa agt tcg
                                                                    144
Ser Ser Asp Leu Val Gln Ser Ala Ile Asp Leu Ile Val Lys Ser Ser
                                                  45
                              40
gtt aaa aaa ctc ttt ttt gac ccc aat caa gtg aat tta caa acc tac
                                                                    192
Val Lys Lys Leu Phe Phe Asp Pro Asn Gln Val Asn Leu Gln Thr Tyr
                         55
                                                                    222
aag cgt tta aat tca gcg ctt ggg gat aag
Lys Arg Leu Asn Ser Ala Leu Gly Asp Lys
                     70
 65
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Asp Asp Arg Ser Phe Phe Ile Thr Asp Ser Arg Tyr Thr Gln Glu Ala
Lys Glu Ser Val Gln Pro Lys Asn Gly Val Leu Ala Glu Val Val Glu
                                 25
             20
Ser Ser Asp Leu Val Gln Ser Ala Ile Asp Leu Ile Val Lys Ser Ser
         35
Val Lys Lys Leu Phe Phe Asp Pro Asn Gln Val Asn Leu Gln Thr Tyr
                         55
Lys Arg: Leu Asn Ser Ala Leu Gly Asp Lys
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ctt ggc tac aac atg gct tta atg gcg atg gtc aat att tta gcc gaa
Leu Gly Tyr Asn Met Ala Leu Met Ala Met Val Asn Ile Leu Ala Glu
                                     10
                  5
  1
atg aaa gcg ttc caa gaa gcc caa aaa aac aac cct aat aac ccc att
                                                                    96
Met Lys Ala Phe Gln Glu Ala Gln Lys Asn Asn Pro Asn Asn Pro Ile
             20
                                                                    108
aac aat caa aaa
Asn Asn Gln Lys
         35
<210> 236
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<213> Helicobacter pylori
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Leu Gly Tyr Asn Met Ala Leu Met Ala Met Val Asn Ile Leu Ala Glu
                                      10
Met Lys Ala Phe Gln Glu Ala Gln Lys Asn Asn Pro Asn Asn Pro Ile
                                  25
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Asn Asn Gln Lys
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Ser Lys Glu Ser Leu Met His Ala Ile Asn Ser Ile Arg Val Gly Met
                                      10
 cat ttt aaa gag ttg agt cag att tta gag agc act att aca gaa agg
His Phe Lys Glu Leu Ser Gln Ile Leu Glu Ser Thr Ile Thr Glu Arg
                                  25
             20
 ggc ttt gtg cct ttg aaa gga ttt tgc ggg cat ggc att ggt aaa aaa
 Gly Phe Val Pro Leu Lys Gly Phe Cys Gly His Gly Ile Gly Lys Lys
 ccc cat gaa gag cca gag atc ccc aac tac cta gaa aaa ggc gtc aaa
                                                                    192
 Pro His Glu Glu Pro Glu Ile Pro Asn Tyr Leu Glu Lys Gly Val Lys
      50
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cct aat agc ggc cct aaa atc aaa gag ggc atg gta ttt tgc tta gag
                                                                   240
Pro Asn Ser Gly Pro Lys Ile Lys Glu Gly Met Val Phe Cys Leu Glu
                                         75
                     70
65
cct atg gtg tgt caa aaa cag ggc gag cct aaa ata cta gcg gat aag
                                                                   288
Pro Met Val Cys Gln Lys Gln Gly Glu Pro Lys Ile Leu Ala Asp Lys
                                     90
tgg agc gtg gtt tca gtg gat ggg ctt aac aca agc cac cat gag cat
                                                                   336
Trp Ser Val Val Ser Val Asp Gly Leu Asn Thr Ser His His Glu His
            100
act atc gcc ata gtt ggc aat aaa gca gtg att ctt acg gag cgt
                                                                   381
Thr Ile Ala Ile Val Gly Asn Lys Ala Val Ile Leu Thr Glu Arg
                            120
        115
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Ser Lys Glu Ser Leu Met His Ala Ile Asn Ser Ile Arg Val Gly Met
                                     10
  1
His Phe Lys Glu Leu Ser Gln Ile Leu Glu Ser Thr Ile Thr Glu Arg
                                 25
             20
Gly Phe Val Pro Leu Lys Gly Phe Cys Gly His Gly Ile Gly Lys Lys
                             40
Pro His Glu Glu Pro Glu Ile Pro Asn Tyr Leu Glu Lys Gly Val Lys
Pro Asn Ser Gly Pro Lys Ile Lys Glu Gly Met Val Phe Cys Leu Glu
                                          75
Pro Met Val Cys Gln Lys Gln Gly Glu Pro Lys Ile Leu Ala Asp Lys
                                     90
Trp Ser Val Val Ser Val Asp Gly Leu Asn Thr Ser His His Glu His
                                                     110
                                105
            100
Thr Ile Ala Ile Val Gly Asn Lys Ala Val Ile Leu Thr Glu Arg
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Gln Leu Ser Gly Gly Gln Lys Gln Arg Val Ala Ile Ala Arg Ser Leu
                                      10
gcg aat tgc cct gat tta ttg ctt tgc gat gaa gcc aca tcc gcg cta
Ala Asn Cys Pro Asp Leu Leu Cys Asp Glu Ala Thr Ser Ala Leu
                                  25
gat tot aaa acc acg cat tot att tta acg ctt tta agc ggc att caa
Asp Ser Lys Thr Thr His Ser Ile Leu Thr Leu Leu Ser Gly Ile Gln
         35
                              40
aaa aag ctt gat ttg agc atc gtt ttc atc acg cat gaa att gaa gtg
                                                                   192
Lys Lys Leu Asp Leu Ser Ile Val Phe Ile Thr His Glu Ile Glu Val
                          55
gtt aaa gaa ttg tgc aat caa atg tgc gtg atc agc agc ggc gaa atc
 Val Lys Glu Leu Cys Asn Gln Met Cys Val Ile Ser Ser Gly Glu Ile
                      70
 65 ·
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 gt
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	50	Leu				55					60					
Val 65	Lys	Glu	Leu	Cys	Asn 70	Gln	Met	Cys	Val	11e 75	Ser	Ser	GIÀ	GIU	80	
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- 1		Lys		5					10					13		96
ggc	ttg	aat	caa	gcc	ctt	gat	aaa	ata	ggc	Com	age	502	yac Nen	Ala	Lve	50
_		Asn	20					25					30			144
gac	tta	cag	aac	ttc	ttg	gat	aaa	acg	act	בננ	999	yar	Tla	Len	Aen	117
		Gln 35					40					45				192
caa	atg	att	gaa	caa	gcc	ccc	tta -	atc	aat	aaa	CCC	710	Cor	Trn	Len	172
	50	Ile				55					60					240
ggt	ccg	cag	gat	ttg	agc	gtt	tta	gtg	aat	atc	gct	tta	dat	age	Tlo	240
Gly	Pro	Gln	Asp	Leu	Ser 70	Val	Leu	Val	Asn	75	Ala	Leu	ASII	Ser	80	288
act	aac	cct	agt	aaa	gag	ctg	act	agc	acc	att	TCL	agc	ata	ggt	yaa Clu	200
		Pro		85					90					90		226
aaa	gcg	tta	aat	gac	tta	tta	ggc	gat	ggc	gta	gtg	aat	aaa	atc	atg	336
Lys	Ala	Leu	Asn	Asp	Leu	Leu	Gly	Asp	Gly	· vaı	vaı	ASN	TAS	TTE	Mec	
			100					105					TIO			384
agc	aat	caa	gtc	tta	ggg	caa	atg	atc	aat	aaa	atc	att	get	gat	aag	204
		115					120					125			Lys	422
ggc	ttt	gga	ggc	gtt	tat	cag	caa	ggt	tta	ggc	tcc	ata	ctg	Dec	caa	432
_	130	1				135					140			PIO	Gln	471
tct	tta	caa	gat	gaa	ttg	aag	aaa	ttg	ggc	atg	ggc	tct				471
Ser	Leu	Gln	Asp	Glu		Lys	Lys	Leu	Gly	Met	GLY	Ser				_
145					150					155						·
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Tyr	Gly	Lys		5					10					13		
Gly	Let		20					25					30		Lys	
_		35					40					45			Asn	
Gln	Met	Ile	Glu	Gln	Ala	Pro	Leu	Ile	Asn	Lys	Leu	Ile	Ser	Trp	Leu	

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55
Gly Pro Gln Asp Leu Ser Val Leu Val Asn Ile Ala Leu Asn Ser Ile
                                         75
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65
Thr Asn Pro Ser Lys Glu Leu Thr Ser Thr Ile Ser Ser Ile Gly Glu
                                     90
                 85
Lys Ala Leu Asn Asp Leu Leu Gly Asp Gly Val Val Asn Lys Ile Met
                                105
            100
Ser Asn Gln Val Leu Gly Gln Met Ile Asn Lys Ile Ile Ala Asp Lys
                                                125
                            120
Gly Phe Gly Gly Val Tyr Gln Gln Gly Leu Gly Ser Ile Leu Pro Gln
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Ser Leu Gln Asp Glu Leu Lys Lys Leu Gly Met Gly Ser
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ggg aat atc acc gtt gat ggg cct tta aga gtg aat aat caa gtg ggt
Gly Asn Ile Thr Val Asp Gly Pro Leu Arg Val Asn Asn Gln Val Gly
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                                     10
                  5
ggt tat gct ttg gca gga tca agc gcg aat ttt gag ttt aag gct ggt
                                                                   96
Gly Tyr Ala Leu Ala Gly Ser Ser Ala Asn Phe Glu Phe Lys Ala Gly
                                 25
             20
acg gat acc aaa aac ggc aca gcc act ttt aat aac gat att agt ttg
Thr Asp Thr Lys Asn Gly Thr Ala Thr Phe Asn Asn Asp Ile Ser Leu
                                                 45
         35
                              40
gga aga ttt gtg aat tta aaa gtg gat gct cat aca gct aat ttt aaa
                                                                   192
Gly Arg Phe Val Asn Leu Lys Val Asp Ala His Thr Ala Asn Phe Lys
                         55
ggt att gat act ggt aat ggt ggt ttc aac acc tta gat ttt agt ggc
Gly Ile Asp Thr Gly Asn Gly Gly Phe Asn Thr Leu Asp Phe Ser Gly
                                          75
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gtt aca ggt aag gtc aat atc aac aag ctc att acg gc
Val Thr Gly Lys Val Asn Ile Asn Lys Leu Ile Thr
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Gly Asn Ile Thr Val Asp Gly Pro Leu Arg Val Asn Asn Gln Val Gly
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Gly Tyr Ala Leu Ala Gly Ser Ser Ala Asn Phe Glu Phe Lys Ala Gly
                                                      30
                                  25
             20
Thr Asp Thr Lys Asn Gly Thr Ala Thr Phe Asn Asn Asp Ile Ser Leu
                              40
Gly Arg Phe Val Asn Leu Lys Val Asp Ala His Thr Ala Asn Phe Lys
                          55
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Gly Ile Asp Thr Gly Asn Gly Gly Phe Asn Thr Leu Asp Phe Ser Gly
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 Val Thr Gly Lys Val Asn Ile Asn Lys Leu Ile Thr
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Gln Lys Val Tyr Asn Asp Ala Gln Lys Ile Ala Asn Ile Ile Ala Ser
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Phe Phe Met Ala Gln Gln Lys Leu Ile Asp Ala Met Ile Asn Ala Arg
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atg	caa	gaa	atc	ttg Leu	caa Gln	aat Asn	cca Pro	ccc Pro	Pro	Pro	Pro	Pro	Ile	· }		010
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Leu	Glu	Val	Leu 20		Tyr	Ile	Tyr	Ala 25	Leu	Lev	Tyr	Ser	Pro	) Asn	Tyr	
-		3 5	Туг	Glu			40	)				40	)		Leu	
	50	1				55	•				60	ı			Ile	
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Ile	Туг	Asp	- Э Туз	r Arg	; Ile	e G13	/ Gly	, Tyr	Gly	Va]	Leu	ı Asp	Lys	з Туг	Leu	

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Lys Asn Pro Glu Asn Tyr Phe Ala Glu Val Glu Gln Ala Ala Phe Ser
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Pro Ala Asn Val Val Pro Gly Ile Gly Tyr Ser Pro Asp Arg Met Leu
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        275
Gln Gly Arg Leu Phe Ser Tyr Gly Asp Thr His Arg Tyr Arg Leu Gly
                                             300
                         295
Val Asn Tyr Pro Gln Ile Pro Val Asn Lys Pro Arg Cys Pro Phe His
                                         315
                    310
Ser Ser Ser Arg Asp Gly Tyr Met Gln Asn Gly Tyr Tyr Gly Ser Leu
                                                         335
                                     330
                325
Gln Asn Tyr Thr Pro Ser Ser Leu Pro Gly Tyr Lys Glu Asp Lys Ser
                                                     350
                                 345
            340
Ala Arg Asp Pro Lys Phe Asn Leu Ala His Ile Glu Lys Glu Phe Glu
                                                 365
                             360
Val Trp Asn Trp Asp Tyr Arg Ala Asp Asp Ser Asp Tyr Tyr Thr Gln
                                             380
                         375
    370
Pro Gly Asp Tyr Tyr Arg Ser Leu Pro Ala Asp Glu Lys Glu Arg Leu
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His Asp Thr Ile Gly Glu Ser Leu Ala His Val Thr His Lys Glu Ile
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 Val Asp Lys Gln Leu Glu His
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 Ser Ile Ile Tyr Pro Leu Tyr Met Gly Gly Ala Arg Phe Thr Met Val
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 cgc att gcg gat ttg atg caa aaa gat gct aat gaa gtg tat cgt ttg
                                                                    96
 Arg Ile Ala Asp Leu Met Gln Lys Asp Ala Asn Glu Val Tyr Arg Leu
                                  25
 aaa aag ctt tcc act ttt caa gag ctt gtg agc gtg tat tac ggc atg
 Lys Lys Leu Ser Thr Phe Gln Glu Leu Val Ser Val Tyr Tyr Gly Met
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 gtg tta aac gca gaa gtg gct gaa act tta gaa gag gtg gaa aaa ggc
                                                                    192
 Val Leu Asn Ala Glu Val Ala Glu Thr Leu Glu Glu Val Glu Lys Gly
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                          55
 cat tat aag cat ttc caa aac gct ttg aaa atg caa aaa gtg ggg caa
                                                                    240
 His Tyr Lys His Phe Gln Asn Ala Leu Lys Met Gln Lys Val Gly Gln
                                          75
                      70
 atc gct agg gta gaa acc tta ggc gct caa gtg gct tat gat aag gcc
                                                                    288
 Ile Ala Arg Val Glu Thr Leu Gly Ala Gln Val Ala Tyr Asp Lys Ala
                  85
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cat	atc	gct	agc	gtt	aag	gct	aaa	gac	gtg	tta	gaa	gtt	tcg	cag	ctc	336
			100					105		Leu			110			
tcg	ttc	aat	tcc	att	tta	tct	agc	aag	gac	gat	tta	gtg	cct	tca	agc	384
		115					120			Asp		125				
aaa	tta	gag	atc	cgc	acg	gag	aaa	aat	ctg	ccc	gat	ctg	agċ	ttt	ttt	432
Lys	Leu 130	Glu	Ile	Arg	Thr	Glu 135	Lys	Asn	Leu	Pro	Asp 140	Leu	Ser	Phe	Phe	
gtt	tct	tcc	acg	ctc	aat	tcc	tac	ccg	gtt	tta	aag	act	tta	gaa	aat	480
Val 145		Ser	Thr	Leu	Asn 150	Ser	Tyr	Pro	Val	Leu 155	Lys	Thr	Leu	Glu	Asn 160	
cag	att	caa	atc	tct	aaa	gaa	aac	acg	aaa	tta	cag	atc	gct	aaa	ttc	528
Gln	Ile	Gln	Ile	Ser 165	Lys	Glu	Asn	Thr	Lys 170	Leu	Gln	Ile	Ala	Lys 175	Phe	•
ttg	ccc	caa	gtg	agt	ttt	ttt	ggc	tct	tat	att	atg	aag	caa	aac	aat	576
			180					185		Ile			190			
tcg	gtg	ttt	gaa	gac	atg	atc	cct	agt	tgg	ttt	gtg	ggc	gtg	gcc	ggg	624
		195		-			200			Phe		205				
cgc	atg	cct.	att	ctt	tct	CCC	aca	ggg	cgc	att	caa	aaa	tac	caa	gcg	672
_	210					215				Ile	220				٠.	
agc	aaa	tta	gcg	gag	ttg	caa	gtg	agt	agc	gaa	caa	atc	cag	gct	aaa	720
225	_				230					Glu 235					240	
aaa	aac	atg	gaa	tta	tta	gtg	aat	aag	act	tat	aaa	gag	acg	ctt	tct	768
_				245					250	Tyr				255		
tat	ttg	aaa	gaa	tac	aaa	agc	ttg	ctt	tct	agc	gtg	gaa	tta	gcc	aag	816
-		_	260					265		Ser •			270			
gaa	aac	tta	aaa	ctc	caa	gag	cag	gct	ttt	tta	caa	ggc	tta	agc	acg	864
		275					280			Leu		285				
aac	gct	caa	gtc	att	gat	gcg	agg	aac	acg	ctt	tct	Con	atc	gtc	gtg	912
	290	•				295				Leu	300					060
gag	caa	aaa	agc	gtg	gct	tat	aaa	tac	atc	gtt	tca	tta	gcg	aat Acn	ton	960
305					310					Val 315					320	1005
atg	gcg	tta	agc	gat	cat	att	gat	tta	Dho	tat	Glu	Dhe	Val	Tur		1003
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	l> 3:															
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			20					25		Asn			30			
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	50	•				55	•			Glu	60					
His			His.	Phe	Gln	Asn	Ala	Leu	Lys	Met	Gln	Lys	Val	Gly	Gln	
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Ile	Ala	Arg	Val	Glu	Thr	Leu	Gly	Ala	Gln	Val	Ala	Tyr	Asp	rys	Ala	

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90
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His Ile Ala Ser Val Lys Ala Lys Asp Val Leu Glu Val Ser Gln Leu
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Ser Phe Asn Ser Ile Leu Ser Ser Lys Asp Asp Leu Val Pro Ser Ser
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                            120
Lys Leu Glu Ile Arg Thr Glu Lys Asn Leu Pro Asp Leu Ser Phe Phe
                                            140
                        135
Val Ser Ser Thr Leu Asn Ser Tyr Pro Val Leu Lys Thr Leu Glu Asn
                                        155
                    150
Gln Ile Gln Ile Ser Lys Glu Asn Thr Lys Leu Gln Ile Ala Lys Phe
                                                         175
                                    170
                165
Leu Pro Gln Val Ser Phe Phe Gly Ser Tyr Ile Met Lys Gln Asn Asn
                                                     190
                                185
Ser Val Phe Glu Asp Met Ile Pro Ser Trp Phe Val Gly Val Ala Gly
                            200
Arg Met Pro Ile Leu Ser Pro Thr Gly Arg Ile Gln Lys Tyr Gln Ala
                                             220
                        215
Ser Lys Leu Ala Glu Leu Gln Val Ser Ser Glu Gln Ile Gln Ala Lys
                                        235
                    230
Lys Asn Met Glu Leu Leu Val Asn Lys Thr Tyr Lys Glu Thr Leu Ser
                                    250
                245
Tyr Leu Lys Glu Tyr Lys Ser Leu Leu Ser Ser Val Glu Leu Ala Lys
            260
                                265
Glu Asn Leu Lys Leu Gln Glu Gln Ala Phe Leu Gln Gly Leu Ser Thr
                                                 285
                            280
Asn Ala Gln Val Ile Asp Ala Arg Asn Thr Leu Ser Ser Ile Val Val
                        295
Glu Gln Lys Ser Val Ala Tyr Lys Tyr Ile Val Ser Leu Ala Asn Leu
                                        315
                    310
Met Ala Leu Ser Asp His Ile Asp Leu Phe Tyr Glu Phe Val Tyr
                                    330
                325
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<220>
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Glu Ile Ile Arg Asp Ile Ala Asp Gln Thr Asn Leu Leu Ala Leu Asn
                                     10
gcc gct att gaa gcc gca agg gcc ggc gag cat ggc aga ggc ttt gcg
                                                                   96
Ala Ala Ile Glu Ala Ala Arg Ala Gly Glu His Gly Arg Gly Phe Ala
                                                      30
             20
gtg gtg gct gat gag gta aga aag ctc gct gaa agg acg caa aaa tcg
                                                                   144
Val Val Ala Asp Glu Val Arg Lys Leu Ala Glu Arg Thr Gln Lys Ser
                             40
ctc agc gag att gaa gcc aat atc aat att tta gtg caa agc att tca
Leu Ser Glu Ile Glu Ala Asn Ile Asn Ile Leu Val Gln Ser Ile Ser
                                              60
     50
gac acg agc gaa agc att aaa aac cag gtt aaa gaa gtg gaa gaa atc
                                                                   240
Asp Thr Ser Glu Ser Ile Lys Asn Gln Val Lys Glu Val Glu Glu Ile
                                          75
aac gct tct att gaa gcc tta aga tcg gtt act gag ggc aat cta aaa
                                                                   288
Asn Ala Ser Ile Glu Ala Leu Arg Ser Val Thr Glu Gly Asn Leu Lys
                                     90
                                                                   296
atc gct ag
Ile Ala
<210> 258
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<212> PRT
<213> Helicobacter pylori
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Glu Ile Ile Arg Asp Ile Ala Asp Gln Thr Asn Leu Leu Ala Leu Asn
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Val Val Ala Asp Glu Val Arg Lys Leu Ala Glu Arg Thr Gln Lys Ser
                             40
Leu Ser Glu Ile Glu Ala Asn Ile Asn Ile Leu Val Gln Ser Ile Ser
                         55
Asp Thr Ser Glu Ser Ile Lys Asn Gln Val Lys Glu Val Glu Glu Ile
                                         75
                     70
Asn Ala Ser Ile Glu Ala Leu Arg Ser Val Thr Glu Gly Asn Leu Lys
                 85
Ile Ala
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<212> DNA
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Ile Gln Ala Leu Leu Val Gly Val Gln Glu Glu Tyr Tyr Ala Ile Pro
                                     10
ctt tct tca gtg tta gaa acc gtg cgc atc agc cag gat gaa att tac
Leu Ser Ser Val Leu Glu Thr Val Arg Ile Ser Gln Asp Glu Ile Tyr
             20
acc gtt gat ggc aag agc gtg ttg cgt ttg aga gat gag gtg ctt tct
Thr Val Asp Gly Lys Ser Val Leu Arg Leu Arg Asp Glu Val Leu Ser
                             40
ttg gtg cgc ctt tct gat att ttt aaa gta gat gct att ttg gaa tcc
Leu Val Arg Leu Ser Asp Ile Phe Lys Val Asp Ala Ile Leu Glu Ser
     50
aac tca gat gtg tat gtg gtt atc att ggc ttg gct gat caa aaa att
                                                                   240
Asn Ser Asp Val Tyr Val Val Ile Ile Gly Leu Ala Asp Gln Lys Ile
                                         75
ggc gtg atc gtg gat tat tta atc ggt caa gaa gaa gtg gtc att aaa
                                                                   288
Gly Val Ile Val Asp Tyr Leu Ile Gly Gln Glu Glu Val Val Ile Lys
                 85
                                     90
tct tta ggt tac tat ctt aaa aac act aga ggc att gct ggt gct acg
                                                                   336
Ser Leu Gly Tyr Tyr Leu Lys Asn Thr Arg Gly Ile Ala Gly Ala Thr
                                                    110
                                105
            100
gtg aga ggc gat ggg aaa atc acc ctt att gta gat gtg ggg gcg atg.
Val Arg Gly Asp Gly Lys Ile Thr Leu Ile Val Asp Val Gly Ala Met
                            120
                                                 125
        115
atg gat atg gca aaa agc atc aag gtc aat atc act acc tta atg a
                                                                   430
Met Asp Met Ala Lys Ser Ile Lys Val Asn Ile Thr Thr Leu Met
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Ile Gln Ala Leu Leu Val Gly Val Gln Glu Glu Tyr Tyr Ala Ile Pro
Leu Ser Ser Val Leu Glu Thr Val Arg Ile Ser Gln Asp Glu Ile Tyr
             20
                                 25
Thr Val Asp Gly Lys Ser Val Leu Arg Leu Arg Asp Glu Val Leu Ser
```

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40
Leu Val Arg Leu Ser Asp Ile Phe Lys Val Asp Ala Ile Leu Glu Ser
                                           · 60
                         55
Asn Ser Asp Val Tyr Val Val Ile Ile Gly Leu Ala Asp Gln Lys Ile
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Gly Val Ile Val Asp Tyr Leu Ile Gly Gln Glu Glu Val Val Ile Lys
                                     90
                 85
Ser Leu Gly Tyr Tyr Leu Lys Asn Thr Arg Gly Ile Ala Gly Ala Thr
                                 105
            100
Val Arg Gly Asp Gly Lys Ile Thr Leu Ile Val Asp Val Gly Ala Met
                             120
        115
Met Asp Met Ala Lys Ser Ile Lys Val Asn Ile Thr Thr Leu Met
                        135
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Lys Ile Gly Val Cys Gly Pro Val Gly Ser Gly Lys Thr Ala Leu Ile
                                      10
gaa gct tta acg cgc cac atg tca aaa gat tat gac atg gcg gtc atc
Glu Ala Leu Thr Arg His Met Ser Lys Asp Tyr Asp Met Ala Val Ile
                                  25
act aat gat att tac acg aaa gaa gac gca gag ttt atg tgt aaa aat
Thr Asn Asp Ile Tyr Thr Lys Glu Asp Ala Glu Phe Met Cys Lys Asn
                              40
         35
 tcg gtg atg cca cga gag agg atc att ggc gta gaa aca gga ggc tgt
                                                                    192
 Ser Val Met Pro Arg Glu Arg Ile Ile Gly Val Glu Thr Gly Gly Cys
                          55
 ccg cac acg gct att aga gaa gac gct tct atg aat tta gaa gcc gta
 Pro His Thr Ala Ile Arg Glu Asp Ala Ser Met Asn Leu Glu Ala Val
                                          75
 gaa gaa atg cat ggc cgt ttc cct aat ttg gaa ttg ctt ttg att gaa
                                                                    288
 Glu Glu Met His Gly Arg Phe Pro Asn Leu Glu Leu Leu Ile Glu
                                      90
                 85
 age gga gge gat aac ett tea geg aca tte aac eea gag eta geg gae
                                                                    336
 Ser Gly Gly Asp Asn Leu Ser Ala Thr Phe Asn Pro Glu Leu Ala Asp
                                 105
             100
 ttt acg atc ttt gtg att gat gtg gct gag ggc gat aaa atc ccc cga
 Phe Thr Ile Phe Val Ile Asp Val Ala Glu Gly Asp Lys Ile Pro Arg
                                                 125
                             120
        115
 aaa ggc ggg cca gga atc acg cgc tca gac ttg ctt gtc atc aat aag
                                                                    432
 Lys Gly Gly Pro Gly Ile Thr Arg Ser Asp Leu Leu Val Ile Asn Lys
                         135
 att gat tta gcc ccc tat gtg gga gcg gac ttg aaa gtc atg gaa agg
                                                                    480
 Ile Asp Leu Ala Pro Tyr Val Gly Ala Asp Leu Lys Val Met Glu Arg
                                         155
                     150
                                                                    497
 gat tct aaa aaa atg cg
 Asp Ser Lys Lys Met
 <210> 262
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 <213> Helicobacter pylori
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 Lys Ile Gly Val Cys Gly Pro Val Gly Ser Gly Lys Thr Ala Leu Ile
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Thr Asn Asp Ile Tyr Thr Lys Glu Asp Ala Glu Phe Met Cys Lys Asn
                             40
Ser Val Met Pro Arg Glu Arg Ile Ile Gly Val Glu Thr Gly Gly Cys
                         55
Pro His Thr Ala Ile Arg Glu Asp Ala Ser Met Asn Leu Glu Ala Val
                                         75
                     70
Glu Glu Met His Gly Arg Phe Pro Asn Leu Glu Leu Leu Ile Glu
                                     90
Ser Gly Gly Asp Asn Leu Ser Ala Thr Phe Asn Pro Glu Leu Ala Asp
                                105
            100
Phe Thr Ile Phe Val Ile Asp Val Ala Glu Gly Asp Lys Ile Pro Arg
                            120
        115
Lys Gly Gly Pro Gly Ile Thr Arg Ser Asp Leu Leu Val Ile Asn Lys
                        135
    130
Ile Asp Leu Ala Pro Tyr Val Gly Ala Asp Leu Lys Val Met Glu Arg
                                        155
Asp Ser Lys Lys Met
                165
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Phe Lys Thr Arg Gln Gly Lys Asp Ile Ala Ile Arg Leu Lys Asp Ala
                                     10
 1
                  5
ccc aag ttg ggg ctc tct caa ggg gat att tta ttt aaa gaa gag aag
                                                                   96
Pro Lys Leu Gly Leu Ser Gln Gly Asp Ile Leu Phe Lys Glu Glu Lys
gaa att atc gcc gtt aat atc ttg gat tct gaa gtc att cac atc caa
Glu Ile Ile Ala Val Asn Ile Leu Asp Ser Glu Val Ile His Ile Gln
                             40
gcc aag agc gtg gca gaa gta gcg aaa ata tgc tat gaa ata gga aac
                                                                   192
Ala Lys Ser Val Ala Glu Val Ala Lys Ile Cys Tyr Glu Ile Gly Asn
                         55
cgc cat gcg gct tta tac tat ggc gag tct caa ttt gaa ttt aaa aca
Arg His Ala Ala Leu Tyr Tyr Gly Glu Ser Gln Phe Glu Phe Lys Thr
                     70
                                         75
65
                                                                   288
cca ttt gaa aag ccc acg cta gcg tta tta gaa aag cta ggg gtt caa
Pro Phe Glu Lys Pro Thr Leu Ala Leu Leu Glu Lys Leu Gly Val Gln
                                     90
aat cgt gtt tta agt tca aaa ttg gat tcc aaa gaa cgc tta acc gtg
                                                                   336
Asn Arg Val Leu Ser Ser Lys Leu Asp Ser Lys Glu Arg Leu Thr Val
                                105
age atg eec cat agt gag eet aat ttt aag gte tea eta geg age gat
                                                                   384
Ser Met Pro His Ser Glu Pro Asn Phe Lys Val Ser Leu Ala Ser Asp
        115
                            120
                                                                   402
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Phe Lys Val Val Lys
   130
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Phe Lys Thr Arg Gln Gly Lys Asp Ile Ala Ile Arg Leu Lys Asp Ala
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		35	Ala	Val			40					43				
	50	Ser		Ala		55					50					
CE	His			Leu	70					10					ov	
Pro				Pro 85					90)		
			100	Ser				105					TIO			
Ser	Met	Pro 115	His	Ser	Glu	Pro	Asn 120	Phe	Lys	Val	Ser	Leu 125	Ala	Ser	Asp	
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1				5					10					10	_	06
	ata	ggc	ttg	ccc	acg	ctt	gtg	gct	aat	gaa	gtg	agc	ggg	atg	aat Aen	96
_			20	Pro				25					30			144
atc	gtt	ttc	caa	agc	gag	aac	ggg	ctg	tta	ggg	att	ggc Gl v	Ala	Tvr	Pro	144
		35		Ser			40					43				100
tta	gag	ggg	agc	gtt	gat	gcg	gat	ctt	atc	aac	gca	gga	aag	gaa	acc Thr	192
Leu	G1u 50		Ser	Val	Asp	Ala 55	Asp	Leu	TTE	ASI	60 A1a	GIY	пуз	GIU	Thr	
ata		~+~	ata	cca	qqc	act	t.ca	ttt	ttc	aat	agc	gcg	gat	tcg	ttt	240
Ile	Thr	Val	Val	Pro	Ğĺy	Ala	Ser	Phe	Phe	Asn	Ser	Ala	Asp	Ser	1110	
65					70					10						288
gcg	atg	att	cgt	ggg	ggg	Cat His	att	gat	Leu	Ala	Ile	Leu	Gly	Gly	atg Met	
				១ភ					90	ļ.				2	•	336
gaa	gto	tca	caa	aat	ggg	gat	Len	get Ala	Asn	Tro	Met	Ile	Pro	Lys	aag Lys	
			1 00	١				105					TIU	,		
ctc	ata	aag		+~	gga	ggg	gct	atg	gat	ttg	gtg	cat	ggc	gct	aaa	384
Leu	Ile	Lys	Gly	Met	Gly	Gly	Ala 120	Met	Asp	Leu	vai	125	GLY	NIC	г пур	422
aaa	gtg	att	gtg	atc	atg	gag	cat	tgc	aac	aaa	tac	ggg	gag	CCT	aaa	432
Lys	Val	Ile	• Val	Ile	Met	GIU 135	HIS	Cys	ASI	груз	140	GLY	Git	. UCI	טונם י	400
gtg	aaa	aag	gaa	tgo	: tca	ttg	CCC	tta	aca	gga	aaa	gge	; gtg	gro	, cat	480
Val	Lys	Lys	Glu	Cys	Ser	Leu	Pro	Leu	Thr	GLy 155	гуу	GIÀ	val	. val	His 160	
145	, 				150		ata	+++	gan			aat	aac	gcc	atg	528
caa	ttg	ata Tir	acq The	, gat · Aen	, cua Len	Ala	yey Val	Phe	Glu	Phe	Ser	Asr	Asr	Ála	Met	
				165					170)				1/3	,	
aaa	tta	gtç	gaa	tta	caa	gaç	999	gto	ago	ctt	gat	caa	gto	, aaa	gaa Glu	576
Lys	Let	ı Val	l Glu	າ Lev	ı Glm	Glu	Gly	vai	Ser	Leu	Asp	Glr	val 190	. Lys	s Glu	
_			180)				185	١.				170	,	•	

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             20
Glu Gly Lys Ile Glu Glu Ala Gln Glu Leu Tyr Leu Lys Val Asn Glu
                              40
Glu Arg Arg Ile His Lys Gln Asn Gly Ser Ile Glu Glu Ala Glu Ile
                          55
Ile Val Ala Lys Asn Arg Asn Gly Ala Thr Gly Thr Val Tyr Thr Arg
                     70
Phe Asn Ala Pro Phe Thr Arg Tyr Glu Asp Met Pro Ile Asp Ser His
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Leu Leu Glu His Val Gln Lys Ala Leu Asn Gln Met Ser Glu Arg Glu
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caa atc ctt atc cag ctt tat tac ttt gaa gag ttg aat ttg agc gag
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Gln Ile Leu Ile Gln Leu Tyr Tyr Phe Glu Glu Leu Asn Leu Ser Glu
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att aaa gag att tta ggc att act gaa tcg cgc att tct caa atc att
Ile Lys Glu Ile Leu Gly Ile Thr Glu Ser Arg Ile Ser Gln Ile Ile
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aat ggc gtg ttt gaa agc agt ggg ggg agg gtg atc ttt gcc att ggt
                                                                   96
Asn Gly Val Phe Glu Ser Ser Gly Gly Arg Val Ile Phe Ala Ile Gly
                                 25
agg gga aaa too tta tta gaa goo aga aac cat got tat gaa atc got
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Arg Gly Lys Ser Leu Leu Glu Ala Arg Asn His Ala Tyr Glu Ile Ala
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caa aag gtg cat ttt gaa ggc atg ttt tat cgc aag gat att ggt ttt
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Gln Lys Val His Phe Glu Gly Met Phe Tyr Arg Lys Asp Ile Gly Phe
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Gln Lys Val His Phe Glu Gly Met Phe Tyr Arg Lys Asp Ile Gly Phe
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Lys Val Leu Asp Leu Lys Glu Tyr Ser
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Met Arg Gly Asp Ala Gln Asp Val Gln Leu Asn Ile Gly Pro Asn Cys
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Asp Gly Phe Ala Ser Arg Asp Met His Ile Val Val Gly Glu Asn Ala
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ccc atc tat tat gac aac acg att tta gat ccc aaa acc acc gac tta
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Pro Ile Tyr Tyr Asp Asn Thr Ile Leu Asp Pro Lys Thr Thr Asp Leu
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gaa agc gaa ggg gtg gat ggg gca gtg agt gaa acc gct agt tct cat
Glu Ser Glu Gly Val Asp Gly Ala Val Ser Glu Thr Ala Ser Ser His
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tta tgc gtg aaa gct tta gcg aaa ggc tca gaa ccc tta ttg cat tta
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Leu Cys Val Lys Ala Leu Ala Lys Gly Ser Glu Pro Leu His Leu
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                            200
      . 195
aga gaa aaa atc gct cgc ttg gtt acg caa acc acc acg caa aag gtt
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             20
Lys Leu Arg Ile Thr Ser Gln Ser Phe Glu Lys Ile His Asn Thr Glu
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Asp Gly Phe Ala Ser Arg Asp Met His Ile Val Val Gly Glu Asn Ala
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Phe Leu Asp Phe Ala Pro Phe Pro Leu Ile Pro Phe Glu Asn Ala His
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Phe Lys Gly Asn Thr Thr Ile Ser Leu Arg Ser Ser Ser Gln Leu Leu
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Tyr Ser Glu Ile Ile Val Ala Gly Arg Val Ala Arg Asn Glu Leu Phe
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Lys Phe Asn Arg Leu His Thr Lys Ile Ser Ile Leu Gln Asp Glu Lys
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Leu Val Asn Cys Pro Ile Glu Leu Ser Gly Val Arg Glu Cys Ile Glu
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Glu Ser Glu Gly Val Asp Gly Ala Val Ser Glu Thr Ala Ser Ser His
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Gly Ser Gly Phe Gly Leu Gly Ser Ala Ile Leu Gly Ser Ala Ala Gly
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gcg att tta ggg agt tat att ggt aat aag ctt ttc aat aac cct aat
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Ala Ile Leu Gly Ser Tyr Ile Gly Asn Lys Leu Phe Asn Asn Pro Asn
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Tyr Gln Gln Asn Ala Gln Arg Thr Tyr Lys Ser Pro Gln Ala Tyr Gln
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cgc tct caa aat tcc ttt tct aaa agt gcg ccc agt gct tca agc atg
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Arg Ser Gln Asn Ser Phe Ser Lys Ser Ala Pro Ser Ala Ser Ser Met
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ggc gga gcg agt aag gga cag agc ggg ttt ttt ggc tct agt agg cct
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Gly Gly Ala Ser Lys Gly Gln Ser Gly Phe Phe Gly Ser Ser Arg Pro
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Asn Gly Thr Ser Lys Leu Val Gln Pro Asn Asn Gly Gly Ser Asn Glu
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Ala Ile Leu Gly Ser Tyr Ile Gly Asn Lys Leu Phe Asn Asn Pro Asn
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 65
gga ggg cgg tgc gag aaa tgc caa ggc gat ggg gac att aaa ata gaa
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Gly Gly Arg Cys Glu Lys Cys Gln Gly Asp Gly Asp Ile Lys Ile Glu
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                 85
atg cac tit ttg cct gat gtg tta gtc caa tgc gat agc tgt aag ggc
                                                                   336
Met His Phe Leu Pro Asp Val Leu Val Gln Cys Asp Ser Cys Lys Gly
                                105
gct aaa tac aac ccc caa act tta gaa atc aag gtg aaa ggc aaa tcc
                                                                   384
Ala Lys Tyr Asn Pro Gln Thr Leu Glu Ile Lys Val Lys Gly Lys Ser
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                            120
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ggc tta ggc tat atc act tta ggg caa aac gct acg act tta agt ggg
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aca ggc aaa acc ctt tat att tta gat gag cct act acc ggt ttg cat
Thr Gly Lys Thr Leu Tyr Ile Leu Asp Glu Pro Thr Thr Gly Leu His
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ttt gaa gac gtg aat cat ctt tta caa gtc ttg cat tct tta gtg gcg
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145	Lys				150			Lys		155					ΤÒΩ
Gly				165				Gln	170					T 12	
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International Application No PCT/IB 00/00603

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C12N15/10 C12Q1/68 C12N1/19 C12N15/31 C07K14/205 A61K48/00 C07K16/12 C12N15/86 G06F17/00 C12N1/21 A61K39/40 A61K39/106 According to International Patent Classification (IPC) or to both national classification and IPC B. FIELDS SEARCHED Minimum documentation searched (classification system followed by classification symbols) IPC 7 C12N C12Q C07K G06F A61K Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched Electronic data base consulted during the international search (name of data base and, where practical, search terms used) EPO-Internal, WPI Data, MEDLINE, CHEM ABS Data, BIOSIS, EMBL C. DOCUMENTS CONSIDERED TO BE RELEVANT Relevant to claim No. Citation of document, with indication, where appropriate, of the relevant passages JAMES R. HUDSON ET AL.: "The complete set 1-43 Y of predicted genes from Saccharomyces cerevisiae in a readily usable form" GENOME RESEARCH, vol. 7, no. 12, December 1997 (1997-12), pages 1169-1173, XP002127444 the whole document Patent family members are listed in annex. Further documents are listed in the continuation of box C. X "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the Special categories of cited documents: "A" document defining the general state of the art which is not considered to be of particular relevance Invention "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone "E" earlier document but published on or after the international filing date "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled *O* document referring to an oral disclosure, use, exhibition or in the art. *P* document published prior to the international filing date but later than the priority date claimed "&" document member of the same patent family Date of mailing of the international search report Date of the actual completion of the international search 1 1 14 00 27 September 2000 Authorized officer Name and mailing address of the ISA

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Montero Lopez, B

International Application No PCT/IB 00/00603

	ation) DOCUMENTS CONSIDERED TO BE RELEVANT	Relevant to claim No.
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Preservant to Classification
Y	WO 97 37044 A (ASTRA AKTIEBOLAG) 9 October 1997 (1997-10-09)	1-3, 7-10, 14-20, 25,26, 30-38, 42,43
	page 2, line 11 - line 25 page 3, line 12 -page 16, line 15 page 16, line 21 -page 18, line 10 page 33, line 33 -page 34, line 14 page 64, line 22 - line 30	
Y	WO 98 26072 A (ELI LILLY AND COMPANY) 18 June 1998 (1998-06-18)	1,2,5, 7-9,12, 14-19, 22,25, 28, 30-37, 40,42,43
	page 2, line 1 - line 25 page 8, line 10 -page 9, line 2	
Y .	EP 0 786 519 A (HUMAN GENOME SCIENCES, INC.) 30 July 1997 (1997-07-30)	1,2,4, 7-9,11, 14-19, 21,25, 27, 30-37, 39,42,43
	page 5, line 41 -page 7, line 7	
Y	BARTEL ET AL: "A PROTEIN LINKAGE MAP OF ESCHERICHIA COLI BACTERIOPHAGE T7" NATURE GENETICS,US,NEW YORK, NY, vol. 12, no. 12, January 1996 (1996-01), pages 72-77, XP002119798 ISSN: 1061-4036 the whole document	1,2,6-9, 13-19, 23-25, 28-37, 41-43
A .	MICHELINE FROMONT-RACINE ET AL.: "Toward a functional analysis of the yeast genome through exhaustive two-hybrid screens" NATURE GENETICS, vol. 16, July 1997 (1997-07), pages 277-282, XP002100296 the whole document	1-43
	-/	

International Application No
PCT/IB 00/00603

C.(Continu	ation) DOCUMENTS CONSIDERED TO BE RELEVANT	Relevant to claim No.
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Delevant in claim 140.
A	ROBERT M FREDERCKSON: "Macromolecular matchmaking: advances in two-hybrid and related technologies" CURRENT OPINION IN BIOTECHNOLOGY, vol. 9, no. 1, February 1998 (1998-02), pages 90-96, XP002127445	1-43
	abstract page 90, left-hand column, paragraph 2 -right-hand column, paragraph 1 page 93, right-hand column, paragraph 2 -page 94, right-hand column, paragraph 1	
A .	WO 96 32503 A (THE GENERAL HOSPITAL CORPORATION) 17 October 1996 (1996-10-17) page 4, line 10 -page 7, line 23 page 18, line 28 -page 20, line 33 page 28, line 28 - line 34 page 29, line 14 -page 30, line 16 page 38, line 29 -page 39, line 25 page 43, line 34 -page 45, line 9 page 57, line 18 -page 62, line 4 page 78, line 19 -page 79, line 4	1-43
A	JEAN-F. TOMB ET AL.: "The complete genome sequence of the gastric pathogen Helicobacter pylori" NATURE, vol. 388, 7 August 1997 (1997-08-07), pages 539-547, XP002062106 LONDON GB cited in the application	44-47, 55-58, 76,77, 79-87
X	table 2 -& DATABASE EMBL 'Online! Accession number 025047, 1 January 1998 (1998-01-01) XP002148640 the whole document	59-75, 83-87

International application No. PCT/IB 00/00603

Box I	Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)
This Inter	mational Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:
1.	Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely:
	Claims Nos.: because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
з. 🗌	Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).
Box II	Observations where unity of invention is lacking (Continuation of item 2 of first sheet)
This Inte	ernational Searching Authority found multiple inventions in this international application, as follows:
	see additional sheet
1.	As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2.	As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. X	As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.: 1-43, 53, 54, 79, 80 and partially 44-47, 51, 55-57, 81-87 (inventions 1,
, [30, 32 and 33) No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is
4.	restricted to the invention first mentioned in the claims; it is covered by claims reco
Remar	the additional search fees were accompanied by the applicant a protest. X No protest accompanied the payment of additional search fees.

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Claims: 1-43

Method for producing a collection of recombinant cell clones usable for two-hybrid systems using genomic DNA from a prokaryotic micro-organism; collection of cell clones so produced; use thereof in yeast two-hybrid systems, kit therefore and recombinant diploid yeast cell so obtained.

2. Claims: Partially 44-47, 51, 55-77, 81-87

Set of two polynucleotide and fragments thereof encoding polypeptide HP0047 of the left column of table I and polynucleotides and fragments thereof encoding interacting ORF's HP0047, HP0048 and HP0695 of the right column of table I; set of two corresponding polypeptides, protein-protein interaction and corresponding complex; computable readable medium having stored such interaction; use of such interacting polypeptides for identifying "selecting interacting domains SID" and SID of SEQ ID NO:68, 70, 72 of Table II and encoding polynucleotides of SEQ ID NO:67, 69, 71 of Table III and homologs thereof; uses thereof as primer or probe; vectors and host cells comprising the same; uses thereof for producing the polypeptides and polypeptides so obtained; uses of the polypeptides in screening assays for for identifying agents capable of modulating such protein-protein interaction; kit therefore and modulator agent so obtained; use of the polypeptides for the modulation of Helicobacter pylori's protein interaction; use for the production of antibodies and antibody so obtained; pharmaceutical compositions comprising any of the above mentioned polynucleotides, polypeptides, vectors, host cells, modulators and antibodies.

3. Claims: Partially 44-47, 51, 55-77, 81-87

Idem as subject 2 for polypeptide HP0061 of the left column of table I and polypeptides HP0066, HP0978, and HP1409 of the right column of Table I; SID of SEQ ID NO:82, 84 and 86 of Table II and encoding polynucleotides of SEQ ID NO:81, 83 and 85 of Table III

4. Claims: Partially 44-47, 51, 55-77, 81-87

Idem as subject 2 for polypeptide HP0064 of the left column of table I and polypeptide HP0063 of the right column of Table I; SID of SEQ ID NO:88 of Table II and encoding polynucleotide of SEQ ID NO:87 of Table III

5. Claims: Partially 44-47, 51, 55-77, 81-87

Idem as subject 2 for polypeptide HP0066 of the left column of table I and polypeptide HP0066 of the right column of Table I; SID of SEQ ID NO:76 of Table II and encoding polynucleotide of SEQ ID NO:75 of Table III

6. Claims: Partially 44-47, 51, 55-77, 81-87

Idem as subject 2 for polypeptide HP0067 of the left column of table I and polypeptides HP0069, HP0609, HP0768, HP0770 and HP0956 of the right column of Table I; SID of SEQ ID NO:196, 198, 200, 202 and 204 of Table II and encoding polynucleotides of SEQ ID NO:195, 197, 199, 201 and 203 of Table III

7. Claims: Partially 44-47, 51, 55-77, 81-87

Idem as subject 2 for polypeptide HP0068 of the left column of table I and polypeptides HP0070 and HP0118 of the right column of Table I; SID of SEQ ID NO:64 and 66 of Table II and encoding polynucleotides of SEQ ID NO:63 and 65 of Table III

8. Claims: Partially 44-47, 51, 55-77, 81-87

Idem as subject 2 for polypeptide HP0069 of the left column of table I and polypeptide HP0067 of the right column of Table I; SID of SEQ ID NO:74 of Table II and encoding polynucleotide of SEQ ID NO:73 of Table III

9. Claims: Partially 44-47, 51, 55-77, 81-87

Idem as subject 2 for polypeptide HP0070 of the left column of table I and polypeptides HP0068 and HP0070 of the right column of Table I; SID of SEQ ID NO:262 and 264 of Table II and encoding polynucleotides of SEQ ID NO:261 and 263 of Table III

10. Claims: Partially 44-47, 51, 55-77, 81-87

Idem as subject 2 for polypeptide HP0071 of the left column of table I and polypeptides HP0278, HP0417, HP0570, HP0775, HP1340 and HP1409 of the right column of Table I; SID of SEQ ID NO:142, 144, 146, 148, 150 and 152 of Table II and encoding polynucleotides of SEQ ID NO:141, 143, 145, 147, 149 and 151 of Table III

11. Claims: Partially 44-47, 51, 55-77, 81-87

Idem as subject 2 for polypeptide HP0072 of the left column of table I and polypeptide HP1489 of the right column of Table I; SID of SEQ ID NO:256 of Table II and encoding polynucleotide of SEQ ID NO:255 of Table III

12. Claims: Partially 44-47, 51, 55-77, 81-87

Idem as subject 2 for polypeptide HP0073 of the left column of table I and polypeptides HP0073, HP0232, HP0259, HP0067, HP0232 and HP0705 of the right column of Table I; SID of SEQ ID N0:154, 156, 158, 274, 276 and 278 of Table II and encoding polynucleotides of SEQ ID N0:153, 155, 157, 273, 275 and 277 of Table III

13. Claims: Partially 44-47, 51, 55-77, 81-87

Idem as subject 2 for polypeptide HP0268 of the left column of table I and polypeptide HP1198 of the right column of Table I; SID of SEQ ID NO:78 of Table II and encoding polynucleotide of SEQ ID NO:77 of Table III

14. Claims: Partially 44-47, 51, 55-77, 81-87

Idem as subject 2 for polypeptide HP0289 of the left column of table I and polypeptides HP0289, HP0887, HP0922, HP1038, HP1543, HP0610 and HP1355 of the right column of Table I; SID of SEQ ID NO:44, 46, 48, 50, 52, 54, 56, 58, 60 and 62 of Table II and encoding polynucleotides of SEQ ID NO:43, 45, 47, 49, 51, 53, 55, 57 and 61 of Table III

15. Claims: Partially 44-47, 51, 55-77, 81-87

Idem as subject 2 for polypeptide HP0311 of the left column of table I and polypeptide HP0312 of the right column of Table I; SID of SEQ ID NO:194 of Table II and encoding polynucleotide of SEQ ID NO:193 of Table III

16. Claims: Partially 44-47, 51, 55-77, 81-87

Idem as subject 2 for polypeptide HP0338 of the left column of table I and polypeptides HP0132 and HP0337 of the right column of Table I; SID of SEQ ID NO:166 and 168 of Table II and encoding polynucleotides of SEQ ID NO:165 and 167 of Table III

17. Claims: Partially 44-47, 51, 55-77, 81-87

Idem as subject 2 for polypeptide HP0391 of the left column

of table I and polypeptides HP0392 and HP0392 of the right column of Table I; SID of SEQ ID NO:258 and 260 of Table II and encoding polynucleotides of SEQ ID NO:257 and 259 of Table III

18. Claims: Partially 44-47, 51, 55-77, 81-87

Idem as subject 2 for polypeptide HP0691 of the left column of table I and polypeptides HP0692 and HP1362 of the right column of Table I; SID of SEQ ID NO:266 and 268 of Table II and encoding polynucleotides of SEQ ID NO:265 and 267 of Table III

19. Claims: Partially 44-47, 51, 55-77, 81-87

Idem as subject 2 for polypeptide HP0697 of the left column of table I and polypeptides HP0012, HP0048, HP0558, HP0599, HP0696, HP0684, HP1037, HP1038, HP1299 and HP1576 of the right column of Table I; SID of SEQ ID NO:222, 224, 226, 228, 230, 232, 234, 236, 238 and 240 of Table II and encoding polynucleotides of SEQ ID NO:221, 223, 225, 227, 229, 231, 233, 235, 237 and 239 of Table III

20. Claims: Partially 44-47, 51, 55-77, 81-87

Idem as subject 2 for polypeptide HP0776 of the left column of table I and polypeptides HP0067, HP0278, HP1378, and HP1409 of the right column of Table I; SID of SEQ ID NO:214, 216, 218 and 220 of Table II and encoding polynucleotides of SEQ ID NO:213, 215, 217 and 219 of Table III

21. Claims: Partially 44-47, 51, 55-77, 81-87

Idem as subject 2 for polypeptide HP0797 of the left column of table I and polypeptides HP0289, HP0887, HP1349, HP1377 and HP1409 of the right column of Table I; SID of SEQ ID NO:184, 186, 188, 190 and 192 of Table II and encoding polynucleotides of SEQ ID NO:183, 185, 187, 189 and 191 of Table III

22. Claims: Partially 44-47, 51, 55-77, 81-87

Idem as subject 2 for polypeptide HP0800 of the left column of table I and polypeptides HP0433, HP0687, HP0800, HP0801, HP0924, HP1267 and HP1460 of the right column of Table I; SID of SEQ ID N0:10, 12, 14, 16, 18, 20 and 22 of Table II and encoding polynucleotides of SEQ ID N0:9, 11, 13, 15, 17, 19 and 21 of Table III

23. Claims: Partially 44-47, 51, 55-77, 81-87

Idem as subject 2 for polypeptide HP0801 of the left column of table I and polypeptides HP0152, HP0800 and HP1513 of the right column of Table I; SID of SEQ ID NO:24, 26, and 28 of Table II and encoding polynucleotides of SEQ ID NO:23, 25 and 27 of Table III

24. Claims: Partially 44-47, 51, 55-77, 81-87

Idem as subject 2 for polypeptide HP0868 of the left column of table I and polypeptides HP0088, HP0327, HP0869, and HP1142 of the right column of Table I; SID of SEQ ID NO:2, 4, 6 and 8 of Table II and encoding polynucleotides of SEQ ID NO:1, 3, 5 and 7 of Table III

25. Claims: Partially 44-47, 51, 55-77, 81-87

Idem as subject 2 for polypeptide HP0874 of the left column of table I and polypeptide HP0875 of the right column of Table I; SID of SEQ ID NO:254 of Table II and encoding polynucleotide of SEQ ID NO:253 of Table III

26. Claims: Partially 44-47, 51, 55-77, 81-87

Idem as subject 2 for polypeptide HP0875 of the left column of table I and polypeptide HP0874 of the right column of Table I; SID of SEQ ID NO:212 of Table II and encoding polynucleotide of SEQ ID NO:211 of Table III

27. Claims: Partially 44-47, 51, 55-77, 81-87

Idem as subject 2 for polypeptide HP0887 of the left column of table I and polypeptides HP0459, HP0610, HP0699, HP0887, HP1157, HP1460, and HP1464 of the right column of Table I; SID of SEQ ID NO:30, 32, 34, 36, 38, 40, 42, 242, 244, 246 and 248 of Table II and encoding polynucleotides of SEQ ID NO:29, 31, 33, 35, 37, 39, 40, 41, 241, 243, 245 and 247 of Table III

28. Claims: Partially 44-47, 51, 55-77, 81-87

Idem as subject 2 for polypeptide HP0935 of the left column of table I and polypeptides HP0072, HP0528 and HP0657 of the right column of Table I; SID of SEQ ID NO:160, 162 and 164 of Table II and encoding polynucleotides of SEQ ID NO:159, 161 and 163 of Table III

29. Claims: Partially 44-47, 51, 55-77, 81-87

Idem as subject 2 for polypeptide HP0978 of the left column of table I and polypeptides HP0979 and HP1583 of the right column of Table I; SID of SEQ ID NO:138 and 140 of Table II and encoding polynucleotides of SEQ ID NO:137 and 139 of Table III

30. Claims: Partially 44-47, 51, 55-77, 81-87

Idem as subject 2 for polypeptide HP1032 of the left column of table I and polypeptides HP0643, HP0818, HP1122, HP1198 and HP1316 of the right column of Table I; SID of SEQ ID NO:122, 124, 126, 128 and 130 of Table II and encoding polynucleotides of SEQ ID NO:121, 123, 125, 127 and 129 of Table III

31. Claims: Partially 44-47, 51, 55-77, 81-87

Idem as subject 2 for polypeptide HP1067 of the left column of table I and polypeptide HP0392 of the right column of Table I; SID of SEQ ID NO:210 of Table II and encoding polynucleotide of SEQ ID NO:209 of Table III

32. Claims: 53, 54, 79, 80 and partially 44-47, 51, 55-77, 81-87

Idem as subject 2 for polypeptide HP1198 of the left column of table I and polypeptides HP0088, HP0268, HP0293, HP0452, HP0705, HP0775, HP0965, HP1032, HP1114, HP1124, HP1198, HP1274, HP1378, HP1411, HP1541 and HP1218 of the right column of Table I; SID of SEQ ID NO:90, 92, 94, 96, 98, 100, 102, 104, 106, 108, 110, 112, 114, 116, 118, 270 and 272 of Table II and encoding polynucleotides of SEQ ID NO:89, 91, 93, 95, 97, 99, 101, 103, 105, 107, 109, 111, 113, 115, 117, 269 and 271 of Table III

33. Claims: Partially 44-47, 51, 55-77, 81-87

Idem as subject 2 for polypeptide HP1230 of the left column of table I and polypeptides HP1230 and HP1529 of the right column of Table I; SID of SEQ ID NO:132, 134 and 136 of Table II and encoding polynucleotides of SEQ ID NO:131, 133 and 135 of Table III

34. Claims: Partially 44-47, 51, 55-77, 81-87

Idem as subject 2 for polypeptide HP1231 of the left column of table I and polypeptide HP1247 of the right column of Table I; SID of SEQ ID NO:120 of Table II and encoding

polynucleotide of SEQ ID NO:119 of Table III

35. Claims: Partially 44-47, 51, 55-77, 81-87

Idem as subject 2 for polypeptide HP1244 of the left column of table I and polypeptides HP0857 and HP1246 of the right column of Table I; SID of SEQ ID NO:206 and 208 of Table II and encoding polynucleotides of SEQ ID NO:205 and 207 of Table III

36. Claims: Partially 44-47, 51, 55-77, 81-87

Idem as subject 2 for polypeptide HP1246 of the left column of table I and polypeptides HP0121, HP0326, HP0407, HP0886, HP1035, HP1244 and HP1460 of the right column of Table I; SID of SEQ ID N0:170, 172, 174, 176, 178, 180 and 182 of Table II and encoding polynucleotides of SEQ ID N0:169, 171, 173, 175, 177, 179 and 181 of Table III

37. Claims: Partially 44-47, 51, 55-77, 81-87

Idem as subject 2 for polypeptide HP1247 of the left column of table I and polypeptides HP1231 and HP1353 of the right column of Table I; SID of SEQ ID NO:250 and 252 of Table II and encoding polynucleotides of SEQ ID NO:249 and 251 of Table III

38. Claims: 52, 78 and partially 44-47, 51, 55-77, 81-87

Idem as subject 2 for polypeptide HP1293 of the left column of table I and polypeptide HP1198 of the right column of Table I; SID of SEQ ID NO:80 of Table II and encoding polynucleotide of SEQ ID NO:79 of Table III

39. Claims: 48 and partially 44-46, 51, 55-57-59, 76, 77, 81, 82, 84-87

Set of two polynucleotides and fragments thereof encoding two Staphylococcus polypeptides; set of two corresponding polypeptides, protein-protein interaction and corresponding complex; computable readable medium having stored such interaction; use of such interacting polypeptides for identifying "selecting interacting domains SID" and polynucleotide encoding SID; uses of the polypeptides in screening assays for for identifying agents capable of modulating such protein-protein interaction; kit therefore and modulator agent so obtained; use of the polypeptides in the preparation of antibodies; antibodies so produced and pharmaceutical compositions comprising any of the above

mentioned polypeptides, polynucleotides, modulators or antibodies.

40. Claims: 49 and partially 44-46, 51, 55-57-59, 76, 77, 81, 82, 84-87

Idem as subject 39 for Streptococcus pneumoniae polypeptides and polynucleotides.

41. Claims: 50 and partially 44-46, 51, 55-57-59, 76, 77, 81, 82, 84-87

Idem as subject 39 for Escherichia coli polypeptides and polynucleotides.

42. Claims: Partially 44-47, 51, 55-77, 81-87

Idem as subject 2 interacting polypeptides not covered by the above mentioned subjects

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